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THE LITERATURE ON THE INTERNAL SECRETIONS. Containing 146 Titles and Articles Reviewed

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OCTOBER-DECEMBER, 1917

EDITORIAL ARTICLES

THE PATHOGENESIS OF THE NEUROSES

THE pathogenesis of disease is quite as important as its pathological anatomy. The study of the changes wrought by disease was of course the foundation of modern medicine and Virchow cannot be too greatly honored for the part he played. The study of the ultimate causes of disease, especially of the bacteria, was of like value and Pasteur and Koch stand with Virchow in the establishment of a scientific medicine. There remains, however, much to be done of a nature as fundamental as that of either group. Thus far we have been halted by our inability to resolve the problem of the connection between material substratum and vital phenomena. And probably the enthusiasm attendant upon the study of the internal secretions is to some extent due to its apparent promise to shed light upon this obscure problem.

Eppinger and Hess called our attention forcefully to the effect of vagus overbalance. Freud has made

us realize that the psyche influences markedly the lower or somatic functions. Pottenger has shown that even the skeletal muscles are influenced by reflexes from visceral lesions. That is, the researches of the past five years have tended to show us the complexity of the interrelation of tissue and nerve. We have, in other words, some more definite illustrations of the well-known principle that usage affects form.

The next step was the work of Cannon when he showed that nerve tone was dependent upon the secretion of the endocrine glands. In other words, that conditions apparently purely nervous in origin were in reality the result of chemical or, if you please, material forces. He showed, however, that such a relationship was reciprocal; and that purely sensory stimuli could stimulate glandular secretion, that is, chemical action.

This demonstrates how complete is the cycle and how difficult it is in a given case to ascertain whether the original cause was psychical or material. In no disease is this more evident than in Graves' disease. Here a succession of nervous shocks may excite the adrenals until the thyroid is put into action, and the threshold of its action permanently lowered—with the attendant phenomena of hyperthyroidism. But again the stimulation of the vagus may come from so material a source as a uterine myoma, or other pelvic irritation—as Hertzler pointed out. But the outcome is the same; the thyroid becomes stimulated until its threshold is permanently lowered.

The importance of these considerations—the importance of realizing that we are dealing with a closed cycle—is evident when we consider the therapy of such condition. For it is obvious that all

cases need not be attacked at the same point or in the same manner. It is evident that by quieting the nervous system we can reduce the force impinging on the endocrine organs. But we may also reduce the disturbance by destroying the glands. Or again we may say that first of all we must remove the original irritant or stimulus, and then quiet the nervous system, or even remove glandular material in order to reduce the quantity of the secretions.

Similar reasoning leads us to hope that in the realm of psychiatry we may secure better definitions and more rounded out conceptions. Thus we may find that Abderhalden is right in believing that dementia precox is the result of a dysfunction of the sex glands —and that the disease may be attacked along lines similar to those in use with Graves' disease.

The conception of chorea as the result of intracranial localization of the streptococcus will at once clarify our vision and materially aid our therapy in that puzzling syndrome.

We might add other illustrations. But these are enough, we think, to enforce our plea for more definiteness in our attack upon this problem, and more clarity in our discussion of the neuroses.

It is evident that the internal secretions form an important link in the chain of events leading up to the obvious phenomena of diseases such as those we have named. And as such they afford us an important point of attack both in our understanding of the processes involved in pathogenesis and in our therapeutic attacks. But they form only one link in the chain. We must not forget their relation to material substrata on the one side, and to nervous stimulation on the other.

THE INTERRELATIONSHIP OF THE THYROID AND THE ADRENALS

DURING the past decade, the subject of pluriglandular syndromy has attracted considerable attention from investigators and clinicians. The thyroid-adrenal interrelation has probably served as the most attractive for study. Together with the recorded observations on this interrelation, have come various dubious conclusions and a considerable amount of theorizing.

Asher and Flack, (1) following up the observation of v. Cyon, (2) that the depressor nerve is more irritable to adrenin immediately after the stimulation of the thyroid nerves (laryngeal) than before, offered the first experimental suggestion of a functional relation between the adrenals and the thyroids. It was also observed that the blood pressure reaction to adrenin was increased after such stimulation. Cannon and Cattell (3) have recently concluded, that the cervical sympathetics, and not the laryngeal, are the secretory nerves of the thyroid glands. Asher and Flack (1) state, however, that they obtained the same results from the injection of thyroid gland extracts as from the stimulation of the laryngeal nerves, hence it is probable that their stimulation included some sympathetic fibers. They found, further, that after extirpation of the thyroid glands, stimulation of the laryngeal nerves no longer caused an augmented reaction to adrenin. They state that the increased rise in blood pressure is not observed unless the depressor nerves are cut. This, the authors think, is a regulatory mechanism by which oppositely directed actions are suspended unless the necessity arises for one or the other to preponderate. They

interpret their results as demonstrating a close relationship between the thyroids and the adrenals.

The phenomena reported by Asher and Flack have recently been subjected to renewed investigation by Levy. (4) It was observed that in cats, after stimulation of the cervical sympathetic nerves, adrenin raises the blood pressure—at times as much as 200 to 300 per cent more than before. Levy further observed that intravenous injections of E. C. Kendall's crystalline substance from the thyroid, in thyroidectomized cats, also produces an augmented adrenin reaction.

Goetsch (5) has recently made the observation that in cases of Basedow's disease, the intradermal reaction to minute doses of adrenin is exaggerated. He also observed that subcutaneous injections of adrenin in these cases greatly increases the symptoms. These reactions, he states, vary directly with the intensity of the symptoms or, as most authors believe, with the amount of thyroidemia. These observations then substantiate the experimental evidence that thyroid secretion serves to sensitize those tissues amenable to the action of adrenin.

A supposition that the thyroid secretion acts as a stimulus to adrenal activity has a number of observations to support it. Ott and Scott (6) have reported that intravenous injections of thyroid extracts increase the adrenin in the blood of experimental animals, but they obtained the same results with extracts of other organs. Hoskins, (7) just prior to this, showed that the administration of thyroid substance to new-born guinea pigs produced hypertrophy of the adrenals. Pregnant adult pigs, similarly fed, however, gave birth to young in which the

average weight of the adrenals was below normal. These apparently paradoxical observations were explained by the suggestion that the blood of the mother, overladen with the adrenal hormones, had inhibited the growth of the fetal adrenals.

Herring (8) later showed that the administration of raw ox thyroid in large doses, to cats, increases the amount of adrenin in the adrenals. There was also found evidence that the weight of the adrenals was increased. Herring (9) later showed that the administration of small doses of thyroid gland to white rats, produces hypertrophy of the cortex and medulla of the glands, with increase of the adrenin content. The hypertrophy of the cortex was found to be somewhat greater than that of the medulla. Accessory suprarenal tissues were also found to undergo enlargement. Herring's work, if confirmed, leaves but little doubt that the thyroid does stimulate the adrenals. Experimental evidence, then, would seem to point to the fact that the thyroid glands act as an activator to the adrenal glands.

There is but little evidence contrary to this. Biedl (10) observed that there was a slight hypertrophy of the cortical part of the adrenals in thyroidless, dwarfed dogs. Pick and Pineles (11) found an enlargement of the adrenals in two goats from which the thyroids had been removed at the age of 6-10 weeks. One of them had been treated with iodothyrin. This evidence, however, is not convincing since no controls were kept and nothing is known regarding the size of the glands before the experiments were begun. Carlson (12) maintains, however, that in young rabbits, after complete thyroidectomy, he invariably observed a marked hypertrophy of the

suprarenals. A satisfactory explanation of the paradox has not been offered.

That the adrenals have a functional reaction on the thyroid glands also has supporting evidence. Osokin (13) observed that repeated injections of adrenin produces marked histological changes in the cells of the thyroid, which he interprets as evidence that adrenin normally stimulates the thyroid to secretion. Cannon and Cattell (3) have shown that injections of small doses of adrenin produce an action current in the thyroid and hence secretory activity in the gland. Stimulation of the splanchnics, leading to adrenal discharge, produces the same results. Levy (4) observed that the injection of adrenin sensitized the vasomotor system to the action of succeeding injections of adrenin. He brings forth evidence to show that this sensitization is due to thyroid discharge produced by the first injection of adrenin. Contrary to these observations, Wiener (14) has reported that injections of adrenin led to storage of thyroglobulin in the gland. The weight of evidence as a whole, however, would seem to indicate that the adrenal secretion stimulates the thyroid gland to secretory activity.

That the thyroid and the adrenal glands each play a role in carbohydrate metabolism, is a well-established fact, which may indicate an interrelation between the two organs. Eppinger, Falta and Rudinger (15) from their work on the relationship between the thyroid and pancreas, arrived at the conclusion, that the thyroid and the chromaffine system, together with, as Falta (16) reported later, the infundibular portion of the hypophysis cerebri, constitute a group of vascular glands which accelerate the

processes of carbohydrate metabolism. The balance they state, is maintained by the antagonistic activity of those other vascular glands, which, like the pancreas and parathyroids, exercise a retarding influence upon the consumption of sugar. They stated that an adrenin injection which, in normal animals, provokes extreme glycosuria together with an increased metabolism of protein in the fasting animal, does not produce glycosuria in thyroidectomized animals, even when sugar is given at the same time. This was confirmed by Grey and de Sautelle (17) with dogs, and by Pick and Pineles (11) with young goats. Underhill and Hilditch (18), however, deny the occurrence of the phenomena in case of dogs. Since there is reason to believe that the thyroid secretion sensitizes the sympathetic system to the action of adrenin and that hyperthyroidism intensifies adrenin glycosuria and hypothyroidism abolishes the phenomena, there remains the possible indication that these glands exert their activity on sugar metabolism via the sympathetic nerves. Schaefer (19) states that the thyroid produces a mobilization of sugar in the body and that thyroid feeding tends to diminish the assimilation limit of sugar. This he states may be due to an increase in the secretion of adrenin or to a direct inhibitory effect on the internal secretion of the pancreas. From the work of Eppinger, Falta and Rudinger, one might conclude that a thyroid-adrenal interrelation plays a large part in the phenomena.

Frankel (20), Broking and Trendelenburg (21), Krause (22) and others, employing different methods, found an increase of adrenin in the blood of patients suffering from exophthalmic goiter, but the

more recent, careful work of Stewart (23) and others has entirely failed to corroborate this finding.

The weight of existing experimental and clinical evidence, then, supports the theories that the thyroid-adrenal interrelation is one of mutual stimulation; that the thyroid secretion sensitizes sympathetically innervated tissues to the action of adrenin, and that they both act on the sugar depots in the body, producing a liberation of carbohydrates.

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METHODS OF INVESTIGATING ENDOCRINE FUNCTIONS

TWO general types of investigation have been widely utilized in the study of the functions of the endocrine organs—augmenting or decreasing in various ways the function in question. In some instances a sequence of the two methods has yielded significant data.

Several different methods of increasing the hormone content of the blood have been employed, such as administration of extracts or organ substance by mouth or in various other ways, grafting into the body viable endocrine tissue or increasing the output from the individual glands as by massage or stimulation of their secretory nerves. Such studies can often be advantageously supplemented by study of human beings or animals in which spontaneous overactivity of the glands occurs.

Functional deficiencies can be created by gland extirpations, by injecting substances to cause bland infarcts in the glands or by ligating the blood vessels supplying the organs in question. Clinical observations of patients with spontaneous or surgical gland deficiencies are also of great value. Indeed, some of our most valuable data has been obtained in this way.

Gland Extracts, Intravenous Injections: Experiments with gland extracts are complicated by the fact that in addition to specific hormones, various more or less potent non-specific substances may be present. When given by mouth these substances are relatively unimportant but when the extracts are introduced by vein they often play a predominant role in the reactions. Cholin, which is a powerful vasodepressant, may be present to some extent in tissue extracts but

it plays a less important part than was formerly supposed. Nucleo-proteins as such have also come to be recognized as unimportant in such extracts. Possibly the well marked reactions that have been reported by certain investigators as due to specific hormones in tissue extracts have been due largely to split-protein toxic products. Largely through the work of Vaughn we have come to recognize that the most harmless protein substances at one stage of their disintegrations give rise to highly toxic bodies. The work of Jobling and Bronfenbrenner has brought out clearly the importance of the tryptic enzymes of the blood itself in forming such toxins. Unless one is on his guard in making gland extracts, these toxins can readily be formed and completely mask any specific reactions obtainable. Anaphylactic shock which apparently is merely a special phase of protein intoxication may enter in as a disturbing factor when the same animal is used in a series of injection experiments. There is ground for believing that even putrefactive products have in the past figured as specific hormones. From the foregoing it follows that the utmost caution must be observed in drawing conclusions from intravenous injection experiments.

The fact that some at least of the hormones will withstand boiling without serious loss of potency affords a means of eliminating the disturbing factors that reside in the protein content of gland extracts. If boiled in weakly acid solution the extract is both sterilized and freed from protein. If the filtrate from such an extract is hermetically sealed or evaporated to dryness it may retain its potency for long periods.

Administration by mouth: This method of introducing gland substances has been of great use clinic-

ally in the thyroid treatment of myxedema and cretinism. Various other examples of oral administration of gland substances are well known. In experimental work the method has been most useful, in the study of the hormone factors in growth. Gudernatsch's well-known experiments on the influence of thyroid substance on tadpoles form a case in point. In such work the possible importance of non-specific substances in the material fed should always be kept in mind. The presence of nucleo-proteins for example may be a determining factor in results. If the experimental animals were not receiving otherwise an adequate supply of protein the administration as gland substance of relatively small quantities of this important food element might cause considerable effect. The researches of Funk, Mendel, McCullom and others show that mere traces of certain as yet unknown food substances may exercise a very profound influence upon growth. These "vitamines" as Funk calls them must always be excluded as the determining factor in results. In all feeding experiments the control animals should be supplied with some indifferent tissue substance equivalent to the gland material administered to the experimental animals or else both should receive a maintenance ration so complete that the addition of the experimental gland substance can play no significant part merely as food.

Another possible source of error in growth experiments resides, according to Robertson, (1) not in the substance fed but in a failure to recognize certain essential features in the process of growth itself. "There is," according to this investigator, "a widespread and mistaken tendency to regard growth as a single process and to infer that if a given substance

or condition accelerates the growth of one particular tissue at any given time, the same substance or condition will also accelerate the growth of other tissues or of the same tissue at a different physiological age. Growth on the contrary is a multiplex phenomenon and factors which favor the growth of one particular type of tissue or the growth of the whole animal at one particular age may actually exert the reverse action upon another tissue or at another stage in the growth of the animal concerned." These facts have an obviously important bearing both upon selecting controls and interpreting any results secured.

Administration by Rectum: The effects of the digestive enzymes upon the endocrine gland substances is largely unknown. In case of the thyroid the fact that ingestion of desiccated gland substance is able to ward off the ill effects of deficient secretion shows that we are dealing with a stable body. In the case of adrenin on the other hand oral administration is largely or quite ineffective. It has been stated that in the case of most of the glands better results are secured by rectal than by oral administration. This possibility should be thoroughly investigated both on account of its clinical bearing and its importance in experimental work.

Parenteral injections: In some instances when fairly rapid but not instantaneous results are desired the gland extracts can be introduced into the intramuscular or subcutaneous tissue spaces. Absorption takes place both into the lymphatics and the blood capillaries. The same is true of extracts introduced into the peritoneal cavity. In this case the absorbative capacity of the omentum is probably of considerable importance. Parenteral injections have certain

advantages: the extracts are spared the possible deleterious action of the digestive enzymes of the alimentary tract; there is less danger to the experimental animal, as from thrombosis, and less disturbance of body functions than when intravenous injections are employed. In case of intramuscular injections the promptness of reaction is little less than when the extracts are given by vein. In case of adrenin the fact that it dilates the blood vessels of skeletal muscle probably accounts to a considerable extent for the rapidity of absorption.

Intrapulmonary injections: That the intrapulmonary route is not without advantages for the administration of adrenin has recently been reported by Auer and Gates. (2) The capillary circulation in the lungs is relatively profuse and the drug is separated from the blood stream only by the thin alveolar and capillary membranes. Absorption is correspondingly prompt. The method would seem to be particularly well adapted to getting adrenin to a failing heart. At the same time the chief danger in the use of adrenin in such cases would probably be avoided, i. e., the danger of inducing fibrillation of the ventricle. When adrenin is introduced directly into the heart it is likely to be carried in too great concentration to the coronary vessels thus causing an over stimulation and the result mentioned. The suitability of intrapulmonary injection as a method of administering other than suprarenal extracts remains yet to be determined. Except possibly for pituitary hormones it would seem not to be desirable.

Intravenous injections: In the case of glands that have a potent internal secretion the most instructive results are usually obtained from intravenous injec-

tions. The hormone is at once distributed throughout the body and the maximal effects are seen before it is destroyed or excreted. Most of our significant data bearing upon suprarenal physiology have been derived from this type of experiment. The method is beset with many pitfalls, however, and a rigidly critical attitude should be maintained in drawing conclusions—an attitude which is conspicuous in much of the literature by its absence. The mere introduction of saline solution into a vein is sufficient to produce as great changes of blood pressure as those that have sometimes been ascribed to a hypothetical hormone in a tissue extract. It should always be borne in mind that an organ extract is composed of many things besides any hormone that may be present. Vasodepressor substances are always found and according to Schaefer, those from different organs show specific variations in their effects upon blood pressure.

Even though a specific substance is shown to be present in a given gland extract the conclusion by no means necessarily follows that it is a hormone that is normally discharged from the corresponding gland. It might be some substance normally accumulated to be destroyed by the gland. It might be some abnormal substance formed during the process of extraction. Particularly is caution demanded in drawing conclusions if other than saline solutions are used in the preparation of the extract. Such a solution is the only menstruum the body has at its disposal and any "hormone" that requires strong reagents for its "liberation" is probably non-existent in the normal gland. More than one elaborate report in the literature if judged thus would be without significance.

Many if not all unboiled tissue extracts contain substances that are likely to induce intravenous coagulation. Kephalin is in this regard particularly important. If massive clotting should occur, death would at once ensue and the only possible erroneous conclusion to be drawn would be that the substance was "toxic." Localized clots, however, may be carried to or formed in the nervous system or elsewhere and produce striking effects that upon superficial consideration might seem to be a result of specific hormones. The inconstancy of such results are, however, sufficient to rule out specificity.

In the investigations of the physiology of the endocrine glands by injection experiments due regard should be paid to the quantitative aspects of the research. When at a single injection as much material is employed as a normal animal could be expected to secrete in several hours no conclusion can be drawn as to the physiological aspects of the hormone in question. At best such a research can afford data of pharmacological value. As a case in point the greatest amount of adrenin that can be obtained from the suprarenals by stimulation of the splanchnic nerve is but one two hundredth of the quantity necessary to produce glycosuria (Osgood). (3) Yet the glycosuric effect of adrenin injections has been made the basis of much discussion as to the physiology of the suprarenal glands. A theory of carbohydrate metabolism prominent a few years since had no more secure foundation than this. The chief difficulty in applying the quantitative criterion in such cases is the marked paucity of reliable data as to how rapidly a normal endocrine gland can secrete. In case of the suprarenals only have we as yet any information.

Neither by direct massage of these glands nor by stimulation of their secretory nerves can more than a moderate rise of blood pressure be evoked. While neither of these methods is exactly equivalent to a physiologic stimulation the fact remains that there is no reason to suppose that the maximal output from the glands is more than a small fraction of the quantities of adrenin injected in many so-called physiological investigations. In view of the fact that reactions to adrenin are known in some cases at least to be exactly reversed with change in quantity the point is of obvious importance.

Direct Application to Tissues: In many cases instructive results are obtained by application of endocrine extracts directly to the living tissues. The clinical use of adrenalin to blanch the nasal mucosa is a well-known procedure that illustrates this method. The adrenalin spray for the relief of asthma is another example. In following this method the tissues are frequently removed from the body and the extracts either applied to the surface or introduced through an isolated artery. Mammalian tissues employed for this type of experiment are kept in warm oxygenated Tyrode's solution or similar fluid; in favorable cases they will survive for hours. Ott and Scott have published many investigations of this nature. In such experiments also the quantity factor should receive due regard. A short segment of gut for example is but a small portion of the total body tissue and would be exposed to a correspondingly small fraction of any given amount of circulating hormones. In individual experiments the dosage should be correspondingly restricted. Just how much allowance should be made for this decreased irritability of the test tissues when

they are removed from the body is as yet unknown.

Organ Grafting: In some instances organ grafting has been used to augment the quantity of circulating hormones. In the early development of the thyroid treatment of myxedema this procedure was successfully employed. There are numerous technical difficulties, however, which limit the use of the method in practical experimentation. The only way in which grafting can be accomplished with anything like constant success is by the employment of the individual's own tissues (autografting) and that method is of obviously restricted utility. The more closely related are the host and the donor of the tissue the more likely is the graft to "take." Transference from one species to another (heterografting) is practically never successful. At best the tissue is soon absorbed and the net result is equivalent to that of a parenteral injection. Grafts ordinarily do not survive unless there already exists a physiological deficiency (Halstead). (4) In most cases the graft acts as a foreign body and stimulates the defensive processes of the host which thereupon destroys it. To secure adequate nutrition to keep the graft alive until it can become vascularized is difficult. Two methods are often employed for this purpose: the tissue is cut into thin slices and these are inserted into some highly vascular tissue such as the spleen. The sex glands seem to be the most easily grafted. Wheelon and Shipley (5) have recently submitted graphic evidence of the functional integrity of testicular transplants. As a method of producing the equivalent of a functional overactivity of any endocrine organ, grafting has as yet not been successful. Possibly in

the future some method of augmenting the tolerance of the host for transplanted tissue will be evolved and lead to valuable results. Up to the present time, organ grafting as an experimental method has been of value chiefly as a check on extirpation experiments.

Nerve Stimulation: In some respects stimulation of the secretory fibers to a given gland is the most satisfactory method of augmenting the amount of the corresponding hormone. The secretion thereby secured is supposedly normal in quality and not greatly outside physiologic limits in quantity. For this among other reasons a definite knowledge of the secretory innervation of all the endocrine organs is needed. In case only of the suprarenal and the thyroid glands is satisfactory information available. Artificial stimulation of the secretory nerves ordinarily involves a considerable degree of trauma as well as anesthesia, both of which detract from the adequacy of the method to reproduce physiologic conditions. To meet this difficulty Cannon has recently employed the method of nerve grafting, using the phrenic as a constantly active source of impulses. The method is technically difficult and was abandoned by Langley years ago after a brief trial as not feasible. Cannon and Fitz (6) have succeeded in several cases, however, in getting results apparently due to functional overactivity of the thyroid gland, when the phrenic nerve was grafted onto the cut end of the cervical sympathetic. These included marked symptoms of hyperthyroidism, particularly augmented basal metabolism. These symptoms subsided when the lobe on the grafted side was removed. The method is theoretically an ideal one to produce pure physiologic augmentation of gland functions under

controlled conditions. The most striking advantage is that there is no question as to what is the primary cause of any effects produced, a question which always arises in a baffling way when cases of spontaneous overactivity of different endocrine glands are studied. It is greatly to be hoped that the technical difficulties may be overcome and the method fulfill the promise it offers of unravelling some of the most puzzling problems in endocrine biology.

Maternal administration: Several years ago a method was proposed to create an excess of hormones in the circulation of developing fetuses by supplying the mother with the corresponding gland, either by feeding or injections. The method offers two theoretical advantages: the experimental animal is treated at the most plastic stage of its existence when maximal effects would be produced and the brunt of the experimental procedure is taken by the mother, which supposedly would be less likely than the young organism to suffer from incidental derangements due to the gland administration. The chief apparent defect of the method is the difficulty of interpreting any results secured. There are present all the possibilities of interaction among the endocrine organs not only of the fetus itself but also of the mother. The actual practical utility of the method has not been adequately determined.

Clinical studies of excessive hormone secretion: Some of the most significant data which bear upon endocrine biology have been obtained in the study of patients suffering from spontaneous overactivity of endocrine structures. The functions of the pituitary organ for instance were completely unknown up to the time Marie discovered the relation of that organ

to acromegaly. Practically all that we know as to the function of the suprarenal cortex is that subjects having enlarged glands are likely to show anomalies of the sex function. Many of our ideas as to thyroid physiology have been derived from a study of Graves' disease—a condition regarded by many as due to simple hyperthyroidism. The chief difficulty in this type of study is to determine what is primary and what are secondary factors. An organ hypertrophy that is taken as a sign of primary overactivity usually can be interpreted equally well as merely an incidental reaction to the same conditions that produce the accompanying symptomatology. The obviously necessary check on this type of study is to produce experimentally the symptoms of the patient by augmenting his supply of the hormone in question. In no case, however, has this as yet been done in a manner entirely satisfactory. Even in case of the thyroid, which seems to be the organ most amenable to this type of investigation, Carlson was unable by the administration of gland substance to produce the clinical picture of exophthalmic goiter either in animals or normal human subjects. Nothing like an experimental acromegaly from pituitary administration has ever been reported.

Endocrine Deficiencies: Several methods of creating endocrine gland deficiencies are known. Some of these are surgical extirpation, producing bland infarcts in the glands, ligating all or part of the blood vessels supplying the structures, injecting boiling water or injurious chemicals into the tissue substance and injection of specific cytolytic sera.

Extirpations: The most common method of cre-

ating a functional deficiency is the obvious one of removing all or part of the gland in question. With the development of modern surgical technique this method has acquired the utmost importance. The earlier investigators, however, had little confidence in results derived from extirpation experiments. Schiff's early observations for instance on the effects of thyroid extirpation were commonly ascribed to suppuration or to injury of important nerves. The method is particularly adapted to investigation of the problem as to what glands are essential to life. But even in this case concordant results have not in all instances been secured. For example Cushing maintains that complete removal of the pituitary gland is inevitably fatal while Aschner, another skilled scientist, is equally sure that animals may survive the operation. One maintains that death following extirpation of the gland is due to incidental trauma; the other that survival when it occurs is to be ascribed to bits of gland left behind in the operation. A serious complicating factor in many cases is the existence of bits of aberrant tissue lying at some distance from the main gland. Accessory thyroids may be found anywhere along the trachea. Outlying suprarenal tissue may be found anywhere along the aorta or even as far away as the epididymis. Parathyroids may occur in various parts of the neck as well as in the thymus. The possible existence of these aberrant structures in any given animal introduces an unavoidable element of uncertainty in many extirpation experiments. Nor will a careful autopsy in all cases determine whether the object of the experiment has been attained. Unless complete serial sections of

all possible tissue that might contain accessory glands are studied they may easily escape detection. Such study is obviously in many cases out of the question.

Infarction: Bland infarcts can be produced by injecting fine suspensions of inert insoluble material into the arteries leading to different glands. Tobacco seeds or lycopodium spores are most commonly employed. This process involves comparatively little trauma and can be regulated to produce various grades of deficiency. It is a method, however, somewhat difficult to control. So far it has not led to any striking results.

Vessel Ligation: Ligating the blood vessels of a given organ in order to decrease its functioning is employed both in clinical and experimental practice. It is a well-known method of treating exophthalmic goiter in patients who are in too precarious a condition to undergo thyroidectomy. For experimental work the method is in most cases unreliable. Small vessels may be left untied and quickly enlarge or capillaries from the surrounding tissue may soon grow into the anemic area and vascularize it so that parts of the gland can hypertrophy and continue to function. In case of suprarenal glands, the loss of which is rapidly fatal, ligation of the blood vessels seems to be essentially equivalent to extirpation.

Interstitial injury: Of the various methods of destroying the tissues by application of injurious materials the injection of hot water is probably the best. The method is relatively safe, no harm being done if the fluid penetrates a blood vessel, whereas in case of chloroform, chromic acid or other escharotics they

are likely to escape into the circulation and produce serious or fatal results. An obvious disadvantage of the injection method is the difficulty of control.

Specific cytolysis: After the discovery of the possibility of producing an increase in the cytolytic power of the blood a hope was entertained that the method would prove valuable in endocrine research. It has been reported that if an animal is given a series of injections of spermatozoa its serum acquires the power of destroying such cells without greatly affecting other kinds. Efforts were made to induce a similar cytolytic power for hormone producing cells as, for instance, those of the thyroid gland. Such a serum might then be injected into an experimental animal and cause the disintegration of its thyroid tissue in situ. The method has not as yet been successfully utilized. The cytolytic sera produced have not been sufficiently specific in action but have destroyed various tissues in addition to those desired.

Clinical studies: Many of the most significant data regarding hormone deficiencies have been derived from careful study of patients suffering from endocrine gland defects. Addison's discovery that deficiency of the suprarenal glands results in muscular and circulatory weakness remains as probably the most significant information yet offered bearing on the physiology of these glands. A similar statement may be made in regard to the discovery of the relation of the thyroid glands to myxedema and cretinism.

In such cases of frank primary deficiency of some one endocrine organ the problem is relatively simple. But as it presents itself clinically the problem is very

frequently complicated by the possibility of interaction among the various glands. A given cause may act simultaneously on several members of a related congeries of organs producing a hypertrophy due to over function in all. But a hypertrophy of one of a related pair may also be due to a vicarious assumption of the function of the other. This is a common interpretation of the pituitary hypertrophy which follows thyroidectomy. When one organ normally exercises a check on another hypertrophy of the second may result from a depression of the activity of the first. If, on the other hand, one organ normally stimulates the other as, possibly, the thyroid does the heart, hypertrophy in the second may be due to overactivity in the first. In view of these different possibilities, to ascribe to any observed phenomenon its actual cause is frequently difficult or impossible.

Moreover primary and secondary causes may be inextricably mingled. In the latter case various obscure "pluriglandular syndromes" may arise. The indefiniteness of the phenomena observable in such cases has led to much speculation and premature theorizing which have to a considerable extent cast discredit upon the recorded data themselves. Such cases should be given the most careful study followed whenever possible by painstaking autopsies. To elucidate this type of disease the conventional "post-mortem" is practically useless. Particular attention should of course be given to the various endocrine glands. The tissues should be fixed as soon as possible after death and subjected to a careful study, using the specific stains with particular attention to mitochondria and other evidences of secretory phe-

nomena. Difficult as is this type of study it offers promise of solving some of the most baffling problems now confronting the endocrinologist.

From the foregoing discussion it appears that research in the field of endocrine biology is beset with pitfalls at every step. In much of the literature of the past the difficulties have been unappreciated or ignored. In a field in which a rigidly critical attitude is indispensable careless credulity has been much in evidence. This is possibly an explanation of the fact that despite an immense amount of patient labor few facts of fundamental importance are unquestionably established. None of the experimental methods applicable to this field of investigation is free from defects. The development of our knowledge has been correspondingly delayed. It is only by the use of all available procedures, checking one against another, that we may hope ultimately to acquire an understanding of the significance of hormone factors, either physiologic or pathologic, in the animal economy.

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ORIGINAL COMMUNICATIONS

ON THE CONTROL OF DIABETES INSIPIDUS BY MEANS OF HYPOPHYSEAL EXTRACT IN A MULTIGLANDULAR ENDOCRINOPATHY (THYREO-HYPOPHYSEO-GENITAL SYNDROME).

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ALL the recent evidence indicates that diabetes insipidus is due to underfunction of the pars intermedia of the hypophysis cerebri rather than to hyperpituitarism as was formerly thought. One of the most brilliant instances of the beneficial effects of a substitution-therapy that we have is the control of the polyuria (and polydipsia) with increase of the concentration of the urine in diabetes insipidus now possible by means of subcutaneous injections of the posterior lobe (and pars intermedia) of the hypophysis cerebri. A number of cases are now on record in which the patients were kept comfortable and excreting a urine of normal amount and of normal specific gravity by injecting 'Pituitrin' or 'Pituitary Liquid'* Until a much larger body of material has been made available for study and for critical judgment, it would seem desirable, for the present, that all syndromes and especially all endocrinopathies associated with diabetes insipidus be reported, especially if a pituitrin-therapy is applied. We must not be too sure that all cases of diabetes insipidus will re-

*For an example of a case thus treated and references to the bibliography, see the paper by Barker (L. F.) and Mosenthal (H. O.) Trans. Ass. Amer. Physicians, Phila. for 1917.

spond as favorably to injections of hypophyseal extracts as have those thus far studied, though should it prove to be true that all cases will respond favorably, a great therapeutic advance will have been made. The case we desire to report illustrates well the effects of pituitrin-therapy in diabetes insipidus in a patient suffering from a multiglandular syndrome.

The patient, Miss M. F., a teacher, aged 33 years, was referred to Dr. Barker for study and treatment by Dr. Kenneth Bradford, of Staunton, Va. She was kept under observation in a nursing-home from July 26th to Aug. 3rd, 1917.

Complaint:—Nervousness; thumping heart; weakness.

Past History:—Well, except for the usual diseases of childhood, until 12. At that age, she fell a distance of about eight feet. There seemed to be no serious injury, and no symptoms resulted from this, though when the menses appeared three years later, the periods were prolonged and painful, conditions that were attributed to the fall. During the next few years the patient had three uterine curettements, a uterine suspension, the ovaries were "replaced" and a double inguinal herniotomy was done. At 28 one tonsil was removed, and at 32 a nasal spur, the latter operation being done for hay fever, which the patient asserts she suffers from during nine months of each year. For four years past the patient had been treated for a mild psychosis, with delusions, and attacks in which she has vague, "far-away feelings", suggestive of an "unreality-complex." She tired easily and could not fix her attention. She has had a tendency to lose weight, has a capricious appetite, complains of palpitation, constipation, and depression at times when she thinks her blood pressure is high. Menstruation is said still to be painful and prolonged unless drugs are used (chiefly calcium and ergot). The patient has had frequent headaches, as well as pain in the back and legs much of the time. She states that her eyes are "weak", and that she has noticed some impairment in hearing for a long time.

Family History:—The patient lives at home, with her father, mother and sister, all of whom are sickly. The sister has suffered from hyperthyroidism.

Present Illness:—For three years the patient has passed from 8-10 quarts of urine per day and has taken large amounts of fluid. The urine has been of very low specific

gravity, but there have never been any casts or other indications of renal disease. The blood pressure has been about 120-140, systolic, and 70, diastolic. The patient says she has passed very large stools at times.

Physical Examination:—Aside from the fact that the patient is fifteen pounds under calculated ideal weight, has a slight gingivitis, a much scarred abdomen, very movable kidneys and hyperactive reflexes, the physical examination was practically negative except for certain changes referable to the glands of internal secretion. These signs, together with points of similar interest taken from the history, may be conveniently grouped in relation to the several endocrine glands, disturbances of which may be regarded as their cause. It is of course recognized that several of these points admit of more than one endocrinopathic explanation, but the following analysis of the symptoms and signs certainly points to an involvement of at least several of the endocrine glands.

Symptoms and Signs Possibly Pointing to the Hypophysis cerebri:—

1. Polyuria and polydipsia, with urine of low specific gravity.
2. Menstrual disturbances: Flow uniformly scanty until past seven years; since then uniformly profuse, often with slight bleeding throughout the entire month over a period of some months; considerable pain in the lower pelvis and in the back at menstrual periods.
3. Acra all prominent; eyebrows very wide apart; slight maxillary prognathism; nails blunt, with no lunulae.
4. Hair on the head very abundant; about normal in the axillae; abundant over the symphysis pubis and reaching in the linea alba nearly to the umbilicus (Typus masculinus); considerable fine hair on legs, especially below the knees.

Symptoms and Signs Possibly Pointing to the Thyroid Gland:—

1. Right lobe of thyroid somewhat enlarged.
2. Slight tachycardia (84-90); palpitation.
3. Fine tremor of fingers.
4. Emaciation (15 lbs. underweight).
5. Slight von Graefe and Moebius signs; eyes prominent.
6. Constipation.
7. Fine skin; gracile fingers.

Many of these points may be taken as indications of some overactivity of the thyroid gland, and yet the patient, even in hot weather, felt somewhat chilly, a condition that, like constipation, is often associated with hypothyroidism.

Symptoms and Signs Possibly Pointing to the Interrenal System:

1. Distribution of hirsuties as given above (Hypertrichosis; Typus masculinus).

2. Marked hypertrophy of breasts and of labia minora.

Symptoms and Signs Possibly Pointing to Chromaffine System:—

No definite signs of disturbance of the chromaffine system are present. There is no abnormal pigmentation. The blood pressure is normal, systolic 130, diastolic 70.

Symptoms and Signs Possibly Pointing to the Pancreas: There is a history of passing very large stools at times.

Certain Physical Measurements:—

Distance from symphysis pubis to floor, 84 cm.

Distance from umbilicus to floor, 96 cm.

Distance from top of shoulder to floor (right side) 134 cm.

Distance from top of shoulder to floor (left side) 136 cm.

Distance from top of head to floor, 162½ cm.

Distance from tip of middle finger to floor, when standing (right), 65 cm.

Distance from tip of middle finger to floor, when standing (left)), 66½ cm.

Distance from middle finger tip of the right hand to that of left hand with arms outstretched, 154 cm.

Weight: 108½ lbs.

Laboratory Examinations.

The patient was under observation for eight days and the following laboratory studies were made:—

Blood:—R. B. C. 4,704,000; W. B. C. 6,600; Hb. 80%.

Differential Count:—

P. M. N.	73.2%
P. M. E.	.8
P. M. B.	.4
S. M.	21.6
L. M.	
Tr.	4.0
	100.0%

R. B. C. and platelets normal. No abnormal cells.

Blood Wasserman: Negative.

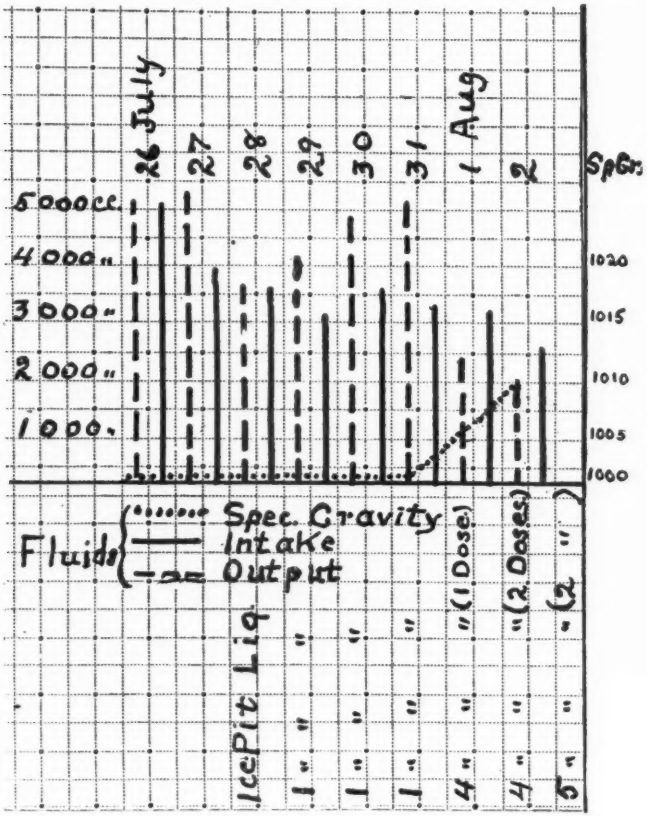
Stool: Negative.

Urine:—The accompanying chart shows the fluid intake and output, and how it was influenced by the administration of pituitary liquid.

Daily examinations of the urine showed a trace of albumin on one or two occasions, but never any casts or blood cells.

For the first two days, the output was about 4700 c. c., parallel with the intake the first day, and exceeding it by nearly 1000 c. c. on the second day. On the third day, therapy

was begun (with unrestricted diet and fluid intake), in the form of 1 c. c. of Armour's pituitary liquid subcutaneously at 9 A. M. daily for four days. On the first day of treatment, intake and output fell to about 3200 c. c. The specific gravity of the urine remained as it had been, at 1002. On the second, third and fourth days of treatment the output gradually returned to its original high figure (4700), the intake, however, being from one to nearly two litres less than the output, and the specific gravity remained at 1002. On the fifth day of treatment a single dose of 4 c. c. of pituitary liquid was given subcutaneously at 9 A. M., and during the next twenty-four hours, the fluid intake dropped from 3100 c. c. to 2700 c. c.,



while the output of urine dropped from 4700 c. c. to 1800 c. c., the specific gravity rising to 1006. On the next day, the same dose was repeated but split, 2 c. c. being given at 9 A. M. and 2 c. c. given at 9 P. M. The fluid intake again dropped, to 2100 c. c.; the output went to 1400 c. c., and the specific gravity rose to 1010. (See chart.) The patient was menstruating at the time and had considerable increase in pain in the pelvis and back for about an hour after each dose. Her general psychic state improved to some extent while under observation, but she was compelled to go home before the studies could be made more complete. It is probable that her thirst and urine can be controlled with smaller doses than those given, provided two doses be given in the 24 hours. Barker and Mosenthal found in their case that 1 c. c. injected twice a day satisfactorily controlled fluid intake, urinary output, and the specific gravity of the urine in a woman who, untreated, passed from 8-11 litres of urine every 24 hours.

Conclusions:

The patient's symptoms point to a diabetes insipidus in association with disturbance of the internal secretion of the hypophysis, the thyroid, the interrenal system, and the gonads. The diabetes insipidus in this case can be controlled by subcutaneous injections of extract of the posterior lobe (and pars intermedia) of the hypophysis.

INTERSEXUALITY AND THE ENDOCRINE ASPECT OF SEX

By Richard Goldschmidt, M.D. (Berl.), New Haven

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ANSWERING the invitation of the editor for a review of the work on sex-intergrades from the viewpoint of endocrinology, we propose to consider in a sweeping form the aspect of the sex-theory as it appears to the author, both in conclusion of his own work and from an open--minded consideration of all the work done upon the different aspects of the problem. In doing so, we think it will become clear wherein the endocrine aspect of the problem enters, and what are its possibilities and limitations.* The more recent work upon the sex-problem started from very different viewpoints and used very different methods, the methods of cytology, genetics, teratology, physiology, serology, endocrinology, etc. The result is a vast amount of information which, if viewed critically and without prejudice in favor of any method of working or thinking, allows us, we are convinced, to assign to every single phase of that research a place within a general conception of sex.

I

The basic problem of sex is the question why a differentiation into two sexes occurs generally in living nature. But this question can not concern us here. We take the fact of the existence of the two sexes for granted. Then the first problem which confronts us is to find what causes normally the distribution of the offspring among two different—often extremely dif-

*A detailed analysis of the problem following the same line of thought as presented here will be given in a book which is ready for publication.

ferent—types of individuals, males and females. This is the problem of the mechanism of the distribution of sex, a problem which is today as completely solved as it is possible within biology. We know that this mechanism is furnished by the existence of two types of gametes in one sex, namely in the male sex, of flies, grasshoppers, mammals, man, and in the female sex of moths and birds, whereas the opposite sex forms only one type of gametes. We know by hybridization experiments that this corresponds closely to the gametic mechanism, which produces the two parental types in equal numbers, when a homozygous form aa, forming only gametes a, is mated to a heterozygous form aA, forming gametes both A and a, the result of the mating being again ½aa and ½aA. We know further by the cytological work of the past fifteen years that the sex-chromosomes (or X-chromosomes) are visible cell elements which correspond exactly in their behavior to the necessities of a sex-differentiator by being present in one sex, the homogametic (XX), in every sex-cell, in the other, the heterogametic sex (XY), in only half of the gametes. We know every phase of the history of these sex-chromosomes and their behavior throughout the life cycle of the two sexes, every single fact pointing to the idea that they really are or carry the sex-differentiators. We may even state, without running the risk of exaggeration, that the theory which regards the distribution of the XX- and XY-combinations to about equal numbers of fertilized eggs as the visible mechanism of sex-distribution, is today so far proven, that the demonstration stands on the level of an experimental proof in physics or chemistry. The main points which justify this conclusion are: 1. The in-

numerable morphological studies, which in every case that proved favorable to study, found the facts about the sex-chromosomes in accordance with the theory. 2. The cytological study of cases of abnormal sex-distribution, as in Aphids, Nematodes, Hymenoptera, Rotifers, where the behavior of the sex-chromosome fits completely the expectation, although very different ways lead to the result. 3. The cytological study of forms like the moth, which had been proven by experimental breeding to be heterogametic in the female sex, whereas all the forms in which the chromosome mechanism had been studied exhibited male heterogametia. As expected those forms were proved to form two kinds of eggs in regard to the X-chromosomes. 4. The facts about the relation of parthenogenesis to sex, of twinning and polyembryony and about sex-mosaics (gynandromorphism) which are all perfectly clear under the aspects of the sex-chromosome theory, but unaccountable otherwise. 5. The study of sex-linked inheritance, which showed that those characters which go in heredity with the sex distribution—both in male and female heterozygosis—follow exactly the distribution of the sex-chromosomes in which they must, therefore, be located. 6. The admirable studies on non-disjunction, which prove that in cases of (visible) abnormal distribution of the sex-chromosomes, all the characters which are known to be sex-linked, show special types of inheritance, which coincide exactly with that abnormal distribution, thus showing beyond a shadow of a doubt their location within the sex-chromosome.

We consider, therefore, in agreement with practically all biologists, whose personal experience in both genetics and cytology give special weight to

their opinion, that the mechanism of sex-distribution is known. Every further construction within the theory of sex has to be built upon this basis.

II

The knowledge of the mechanism which distributes in the right way those things which are responsible for the ultimate differentiation of male and female sex might be compared with information about the system of tracks and switches within a railroad station, which direct the trains into their different directions. But this knowledge does not furnish any information about the material, the destiny, the loads, or the moving power of the trains. So the next problem in regard to sex is to find out what is moved by the distributing mechanism and how it brings about the differentiation of one or the other sex. The problem of the mechanism of sex-distribution is followed by the problem of the physiology of sex-differentiation. The answer which is usually given as a solution of this problem is, that the sex-chromosomes carry a Mendelian factor, a sex-differentiator. But this solution is not satisfactory, first, because of being only formal and symbolic and referring the question to another unknown quantity; second, because, when worked out in detail, it leads into difficulties, which long since have convinced many cytologists and geneticists that not only the quality of the sex-factor but the quantity of the X-chromosome-substance must be the decisive fact; third, because we can not get around the fact that both sexes contain the anlagen of either sex, which can make their visible appearance irrespective of the gametic or zygotic constitution of the individual under certain experimental

conditions. We believe that these difficulties have been overcome now and the way towards a physiological understanding of sex-differentiation been cleared by the work on inter-sexuality.*

III

In order to make clear the relation of the facts of intersexuality to the mechanism of sex-distribution on one side and to the hormonic aspect of sex-differentiation on the other, one point has to be called first to the attention. We know that, in the animal kingdom at least, two types are found in regard to the differentiation of sex-characters (probably also in other processes of growth and differentiation). The one type present in insects, excludes the participation of endocrine activities of the sex-glands in the process of sex-differentiation. Castration or transplantation and transfusion experiments with gonads, blood, body extracts are without influence upon the differentiation of sex-characters. The decision is irrevocably reached at the moment of fertilization. (1) In the other group, however, including birds and mammals, the differentiation of the sex-characters is linked with the endocrine activities of the sex-glands, exactly as growth and metabolism are linked with other endocrine organs, as is proved by the well-known results of castration and transplantation. It is clear that it will be easier to derive the basic conceptions from the simpler case of insects. (2)

Our experiments, performed with races of the gipsy-moth, have enabled us to get under perfect ex-

*We have proposed the use of the terms intersexe, intersexual, intersexuality instead of sex-intergrades because the former terms can be used in all scientific languages, whereas the latter must be translated, e. g., Sexuelle Zwischenstufen" in German.

perimental control the production of intersexuality. (3) By building up definite combinations of races by means of cross breeding, we are able to produce without failure and in the expected numerical relations every single intergrade leading from a normal female to a male or vice versa, the end points, of course, being the complete transformation of a (genetically) would-be female into a male and a would-be male into a female. Without going into details, we might point to some steps in the analysis of the phenomenon, which justify the conclusions in regard to the problems of this essay. The normal mechanism of sex-distribution in this moth is that of female heterogametia, fertilization resulting in about equal numbers of male and female offspring. All of the races involved behave perfectly normally in this respect. But whereas certain crosses between different races are also normal, others invariably give an abnormal result: the cross A-female times B-male gives normal offspring, but B-male times A-female gives all males normal, all would-be females intersexual. In other crosses with other races the opposite happens,—all males are intersexual, all females normal. It could be shown then that the degree of resulting intersexuality is constant for a given combination; e. g. the female of race A will give all normal offspring with a male race M; but with the male N all would-be females will be slightly intersexual, exhibiting certain male characters; with the male O, all would-be females will be intersexual midway between the two sexes; with the male of race P, all would-be females will be high grade intersexuals, almost transformed into males; and with the male race Q, only males will be produced, although half of them are genetically

females. If we breed now another race B as female to all these males a similar series will be produced, but it might reach with the male O the point of complete transformation of all would-be females into males.

These facts and their further genetic analysis show that every individual is able to develop into one sex or the other or any stage between; further that every individual contains all the elements necessary for the development of either sex and its attributes; further that these elements or substances must have a certain quantitative relation to each other in order to secure to one of them the control of development; and that the introduction of quantities in a cross which do not fit the given quantity of the other partner set up the sex-differentiation in favor of the higher quantity. The analytical experiments proved then that the substances which control male differentiation follow the distribution of the sex-chromosomes and must therefore be considered to be carried by them. Whereas the substances controlling female differentiation are always transmitted maternally, that is, from mother to egg. From this it follows, that the mechanism of distribution of the sex-chromosomes results (in the case of female heterozygosis) in distributing to half of the fertilized eggs twice the quantity of the substance which causes male differentiation as to the other half, whereas the substance for female differentiation is constant in all cases. And as the tide of differentiation can be changed in favor of one sex and in a quantitatively increasing series, without any change in the mechanism of the chromosome-distribution it follows, that irrespective of this constitution the decision lies with the respective ab-

solute quantities of the two sex-substances; the greater quantity wins more or less completely.

But how can we conceive that the greater quantity acts in determining one sex or an intergrade between the two sexes? A careful analysis of the intersexual individuals has given the clue. In studying the different types of male or female intersexuality, we find that not every organ exhibits a definite type between the two sexes, say all of them half or one third between the characters of the sexes. The grade of intersexuality is, moreover, a statement applying to the condition of the animal as a whole. But the different organs are not alike. One organ is already say completely male, another still female, a third female at the base, male at the end. Now it could be proven that the organs or parts of organs which become first changed towards the opposite sex are the ones which are last in embryonic development and the ones which are transformed only in the last steps of intersexuality are the first differentiated embryologically. For example, the sex gland, which is differentiated very early, is transformed into a gland of the opposite sex only when all the somatic organs are already changed. And it is shown from the complete analysis of such facts, that in case of female intersexuality—the other way in male intersexuality—all organs develop female up to a certain turning point, when suddenly the development proceeds under the aspects of male differentiation. Therefore all organs differentiated when the turning point occurs are female, the ones which differentiate later are male, and the ones differentiated over the entire period start female and end male. Thus the degree of intersexuality is determined by the more or less early position

of the turning point in development. There we have a time coefficient coordinated with the quantitative differences in the amount of sex-differentiating substances, i. e., these are substances which increase the velocity of a reaction proportional to their quantity. It seems safe therefore to ascribe to them at present the character of enzymes.

The complete analysis of experimental zygotic intersexuality—zygotic because the result is determined at the moment of fertilization—has taught us then what the mechanism of sex-distribution by means of the sex-chromosomes means physiologically: the adjustment of the relative quantities of male and female enzymes, thus assuring to one the greater velocity of reaction. But there is now a limit to our analysis. We see no means of ascertaining what kind the reaction is which is brought about, or, in the language of chemistry, the velocity of which is influenced by the concentration of the enzymes. But the answer can be given, we believe, by the facts about hormonic intersexuality.

IV

It is well known to every student of biology and physiology that in the higher vertebrates, at least birds and mammals, the endocrine function of the sex-gland plays an important role in the development of secondary sex-characters. Early castration in mammals prevents the normal development of the visible characters, and results in the assumption even of the male secondary characters by female birds. Successful early transplantation of the heterologous gonad makes either sex assume to a more or less complete degree the characters of the other sex. (4) We might call this already the production of hormonic

intersexuality, which of course appears only in those organs which are physiologically able to change under the influence of hormones, irrespective of the genetic constitution in regard to sex. But the methods which have to be used exclude a complete experiment in intersexuality, where the entire body, including sex-glands, ducts, etc., must react. Fortunately nature has performed such an experiment for us, as F. R. Lillie's recent analysis of the case of the free-martin has revealed. (5) Among twin calves, cases of normal male and female are very rare. If both are not of the same sex, in most cases a normal male is combined with an abnormal "hermaphroditic" female, the freemartin. It is now proven that this freemartin is a typical case of hormonic intersexuality. Lillie could show that in this—and only in this—case an anastomosis between the blood vessels of the twins occurs, so that the same blood flows through both. In the male partner, the testis, with its interstitial tissue, develops first, when the ovary of the female has not yet reached the stage of endocrine function. So the female comes under the influence of the male hormones, the ovary stops differentiation and all the sex-characters develop further in the male direction. The result is the freemartin, a calf with very much female external sex-organs, almost male sexual ducts and a sex-gland containing sperm tubules but without spermatogenesis.

If we compare now this case of true hormonic intersexuality with the zygotic intersexuality of the moth, we see at once that the "turning point" from which sexual differentiation changed in the latter case corresponds exactly to the moment in the case of the freemartin, when the male hormones are

poured into the blood of the female. Comparing the facts carefully we feel justified therefore in giving the following answer to our former question: Of what kind is the reaction accelerated by the action of the sex-enzymes with a velocity proportional to their concentration? The reaction is the production of the specific hormones of sexual differentiation. In insects this occurs in every single cell of the body as an irreversible consequence of the combination in fertilization. In the higher vertebrates the reaction becomes more or less centralized within the interstitial tissue of the sex glands.

We have purposely dismissed with a few general words the work on castration and transplantation in birds and mammals in order not to interrupt our general line of argument. But we must now draw attention to the fact that some complication comes in here which is not at present completely understood. We mean the complexity of the action of the hormones of the sex-gland on one side and their relation to the genetic (chromosomal) constitution of the cells upon which they act. We have pointed out that the action of these hormones is required when the sex-characters are to differentiate normally. This fact is proved by the castration experiments in mammals, resulting in the failure of further sexual differentiation, and, furthermore, by the case of the freemartin. But there exists another activity of the hormones of the sex-gland, namely the inhibition of the sex-characters of the other sex. This is proved by the cock-feathering of old female birds and the fact that castration in female birds makes them assume the characters of the male sex. And this shows again that in these higher vertebrates sexual differentiation is possible without

specific hormonic action. The latter point is further proved by the fact that in birds typical bilateral gynandromorphs exist, that is, birds with female characters on one side and male characters on the other side of the body. We know from the study of gynandromorphs in insects that they are produced by an abnormality in the distribution of the chromosomes, resulting in the presence of the female set in one half of the body and the male set in the other half. In these gynandromorphous birds the hormones, whatever they are, must be present everywhere in the body; if they were the exclusively decisive factor, no gynandromorphs would occur. To make the case still more complex, gynandromorphic birds are known with an intricate pattern of male and female characters (7); and finally, others are known which, together with the rhythmical change of sexual plumage during one of the breeding seasons, exhibit in certain feathers a mosaic-like admixture of the characters of the other sex. And finally we have the case of the Sebright-Bantams, fowl where the roosters are normally hen-feathered. But when these roosters are castrated they develop normal cock-feathering! (8) No doubt this short account already shows the existence of an immense complexity, which cannot be regarded as easily to be disentangled. But we may state in what manner we think the facts may be brought together. We assume that in birds the genetic situation is the same as it is in insects. From the moment of fertilization, every cell contains the two enzymes of sexual differentiation which, in proportion to the quantity in which each is present, accelerate within every cell the production of the hormones

of sexual differentiation. But there is one principal physiological difference between the insects and birds: in the former the embryonal and larval development ends with one short period of sexual activity after which the animal dies; in the latter, however, a comparatively long period is necessary before the condition of sexual maturity, which then lasts for several years, is reached. If the conditions were alike in the two cases, then every bird would change its sex during its lifetime, that is, it would become intersexual when the amount of the hormones of the other sex within the cells reached a certain mark. This is, however, prevented by the additional phenomenon of the endocrine production of an inhibitory hormone for the characters of the other sex. This specific endocrine function is based on the presence of a sex-limited or, as we prefer to say, sex-controlled factor, as can be deduced from Morgan's Sebright-Bantam crosses. Thus we may account, at least in principle, for the cases in birds, although additional hypotheses will be necessary for special cases like the Sebright-Bantams or the rhythmical breeding-plumage of some birds.

In mammals, however, a further advance seems to have been made in the direction of centralization of the control of the process of differentiation. Here the production of the hormones of sexual differentiation seems to have been shifted from the individual cells to a special endocrine organ, the interstitial tissue of the sex-glands,—a fact most convincingly shown in the case of the freemartin. Castration alone, therefore, can not induce the development of the other sex-characters; that can be accomplished

only by the transplantation of heterologous gonads. And gynandromorphism seems to be impossible. Finally we repeat that these views can be regarded as provisional only and that much experimental work is still needed here.

V

Although no other cases of zygotic and hormonic intersexuality are known, where a complete genetic and embryological analysis was possible, the phenomenon will certainly be produced in many other cases. Collectors of insects have often described freaks, which probably are intersexual individuals (not to be confused, however, with gynandromorphs, which are a very different thing); and at least one instance is known where some of the steps produced in our experiments could be duplicated, as in Harrison's crosses of species of the moth Biston. Another instance is found in Daphnids, where Banta (9) found recently a strain throwing constantly intersexuals through many generations, although no experimental control was yet possible. Further the teratology of birds, mammals and man has furnished a considerable number of cases of so-called hermaphroditism and pseudohermaphroditism, many of which are probably cases of hormonic intersexuality, (10) judging from a comparison with the freemartin.*

*Some authors claim that the presence of perverse mating instincts is a type of intersexuality. Halban and others claim it for the case of man, Riddle for cross-bred pigeons, which are supposed to exhibit the perversion more regularly than normal pigeons do, as well as dogs, cows, etc. The possibility of such an explanation can not be denied; but the claim can only be regarded as justified when it is shown that perverted sex-instincts, though permitting also a normal mating, and combined with complete normality of primary and secondary sex-organs, are the starting point or end point of a graduated series of somatic intersexuality. No such evidence is yet available and the behavior of those instincts in intersexual moths—the only completely analyzed instance—is not in favor of such a view.

But there are other instances of abnormal sexuality known which we feel justified in considering as further types of intersexuality and which will throw further and important light on the problem. There is first the important case of the Gephyrean worm, Bonellia, as analyzed by Baltzer. (11) Bonellia is well known as the prototype of extreme sexual dimorphism: the female is an animal with a plum-like body to which a very long proboscis is attached, the male is a minute animal of the size of an infusorium, with a rudimentary organization, living within the uterus of the female. If a young larva attaches itself to the proboscis of an adult female and lives there "parasitically" for some time, it develops invariably into a male. Otherwise the larva stays in an indifferent state for some time and then becomes female in the majority of cases. If, however, the experimenter interrupts the "parasitic" stage at different times, individuals develop with different mixtures of male and female characters, that is, intersexual individuals. But there are a few more details which are important for the interpretation of the case. Among the larvae which develop into females, the ones which are late in development, form first sperm, before they become female. Further, a short stage in the parasitic condition accelerates development though it might be female. Then the combination of male and female organs in the intersexes is not orderless, but it seems that the stage of differentiation at the moment of the "turning point" (the interruption of parasitic life) determines the combination. Here we see at once a parallel to the other cases of intersexuality, which suggests the following interpretation: If we wanted to make a decisive experimentum crucis in

regard to the theory of the quantitatively regulated sex-enzymes, it would be, to find a method which accelerates or retards the velocity of growth and differentiation of the individual without influencing the velocity of reaction of the sex-enzyme. Such a method would enable us to force the processes of differentiation into the time when the male or female hormones are set free and therefore to make any individual as intersexual as we like. It seems that Bonellia performs this experiment, furnishing the acting substance by the secretion of the proboscis. The interpretation of the case would be, therefore: In the fertilized eggs of Bonellia, which probably are genetically alike, the relation between the velocity of reaction of the sex-enzymes and the velocity of embryonic differentiation is such that a very slow rate of differentiation is confronted with a system of sex-enzymes possessing a high concentration of the male and a low concentration of the female enzyme. In normal development, the time of differentiation of most organs lies beyond the point of the late production of female hormones and the animal is therefore female. The function of the secretion of the proboscis is an acceleration of the rate of differentiation, just as, for example, the hormones of the thyroid act upon the metamorphosis of the frog; differentiation then falls within the time of action of male hormones, the female hormones not yet being present at all. And an incomplete acceleration of the rate of differentiation produces intersexuality, i. e., differentiation first under male then under female hormonic conditions. We might therefore call this type intersexuality by activation. The secretion of the proboscis, activating the rate of differentiation, might be regarded as hor-

monic (although exocrinic) just as the similar action of the thyroidea. It need hardly be added that this hormonic function has nothing to do with the sex-hormones.

Another phenomenon should at least be mentioned in this connection,—the so-called protandric hermaphroditism of parasitic crustacea and certain molluscs. In the case of crustacea the simplest type—many others exist—is that the individual develops as a male and later, after having fulfilled as such his functions, begins a parasitic life and is transformed into a female. (12) Gould (13) has described a very similar case in the mollusc Crepidula plana, although no parasitism is here concerned. His experiments, however, show that the development of the male phase of an individual is induced by the presence of larger individuals of either sex. Even female individuals may develop male organs to a certain extent under such circumstances. A similarity is certainly exhibited here to the case of Bonellia, although the details are not so clear.

VI

There is another case of intersexuality which has to be regarded as a special case of zygotic intersexuality. This is the case of the frog, as analyzed by R. Hertwig and his students. (14) Here it is possible to produce by certain combinations of races (some races exhibit the same phenomenon in nature) animals which have first an ovary which is gradually changed into a testis during development. We refrain from reporting the complicated details of the important work, as there is no other endocrine aspect of this case of "transitory intersexuality" than the one common to all cases of zygotic intersexuality.

But another type of intersexuality can not be passed by, the intersexuality as consequence of parasitic castration, because it has been used as a starting point of attack against the hormonic interpretation of sex. (15) The male crab Inachus, if parasited by Sacculina assumes secondary sex-characters of a female and even eggs are formed within the testis. This is, of course, male intersexuality. But the parasited female does not change correspondingly. G. Smith, who analyzed this case, sees the cause of this change of the male towards femaleness in the influence of the parasite upon the fat-metabolism of the host, the metabolism assuming the female type. He doubts, therefore, an endocrine influence upon sex-differentiation and adheres to a theory of metabolic stimulation. The parasite as well as the presence of the ovary push the metabolism in the direction of fat-production, as can be demonstrated. Fat constitutes the nutritive material for the eggs and therefore the male sex-cells in the parasited animal grow into eggs.

The last conclusion can be disproved by some facts from our experiments in intersexuality. The normal female caterpillar stores vast amounts of fat, which are used in building up the eggs during pupal life. If now female intersexuality is of such a type that the turning point coincides about with the time of pupation the animal has the large abdomen of the female with all its nutritive material. But then male differentiation begins and no eggs develop in the ovary, which does not grow beyond the larval stage. The hatching intersexual female then possesses the large female abdomen filled with blood rich in fat which could nevertheless not induce the young eggs

to grow and fill out the abdomen; the presence of the male hormones after the turning point preventing it.

We further fail to see how the facts about parasitic castration could be used against the endocrine aspect of sex-differentiation. A different type of metabolism in regard to the sexes is well known for many classes of animals, even a different protein specifiicity, as shown by precipitin reactions. There is no reason for putting this difference upon another level than that of other sex-characters, but for the assumption that the hormones of sexual differentiation act upon the morphogenetic processes by the intermediary of a metabolic change. In view of the fact that all endocrine substances including those of the sex-glands, act in some way upon the general metabolism, such an assumption is certainly justified. And it would be in harmony with other physiological facts, e. g., the striking change of the type of metabolism in flies with the metamorphosis, according to Weinland (16) as compared with the influence of the thyroid on starting metamorphosis in frogs. (17) But this is a problem which concerns every phase of the physiology of development and the question of hormonic participation in the process.

We can hardly pass this metabolic aspect of our problem without referring shortly to views, which, in spite of some points of contact, seem to be in contradiction to the views which we derived from our work. We mean the work of Whitman and Riddle and Riddle on pigeons. (18) Riddle has revived the metabolic view of sex-determination which was held in pre-Mendelian, prechromosomal and prehormonic times. He assumes that the metabolic condition of the egg is responsible for the differentiation of sex.

The material on which he bases his views is genetic as well as physiological. The main genetic fact is, that from a family-cross of doves only males, and from a generic cross nearly all males are produced. But if reproductive overwork is forced upon these birds the early eggs produce mostly or only males, the later eggs mostly or only females. The chemical study of the eggs showed that their metabolic state or energy-content is correlated with the sex of the future animal in normal reproduction as well as in the above mentioned experimental conditions. Riddle seems therefore to believe that these metabolic conditions of the eggs are the basis of sex and controlling these conditions means the control of sex. In looking over all the facts regarding the mechanism and physiology of sex, we feel unable to agree with such a theory, although realizing the importance of the actual facts. One and the same egg of a Rotifer or a bee can develop into a male or female, the decision lying with parthenogenesis or fertilization; the same egg, however, can develop into a gynandromorph or mosaic of male and female parts of any mixture if fertilization is abnormal (the famous Eugster bees). (19) And nevertheless male and female bees are as different in regard to metabolism as any other animal on record (see Straus). (20) One and the same egg of the gipsy moth develops into a female, an intersexe of any description, or a male, the result depending exclusively upon the genetic constitution of the fertilizing sperm, viz., the sex-chromosomes of the sperm, as can be proven with mathematical certainty. In every case of male heterozygosis the situation is the same and the metabolic differences of the sexes are the consequence of the combination in fer-

tilization, not the cause. We feel justified, therefore, in rejecting a theory of sex, which makes metabolic differences the cause instead of one of the effects of sex-differentiation. We think, moreover, that the importance of that work on doves lies in another direction.* It might belong to the same category of sex-problems as the overripeness experiments of Pflüger, Thury, Hertwig, etc., as the relation of the visible differences in egg-size of Dinophilus to sex, as the problem of male- and female-producers in Aphids and Hymenoptera; the problem of influencing the chromosomal mechanism of sex-distribution; a problem which is certainly of the greatest cytological, physiological and practical interest.

VII

We have tried to sketch the theory of sex as we see it, as the result of the different lines of research and our own work, and to assign to the endocrine aspects of the problem the right place within. We can hardly finish this very condensed review without pointing to the possibility of applying the same line of argument to the problem of heredity in general.* (26) There is no logical reason for separating the difference in regard to sex from the other specific differences in living nature. The characters which distinguish sex are of the same order as the characters which separate species, genera, families. They are size and shape, symmetry and subdivision, and all the results of differential growth; they are chemical qualities like pigmentation, and all the phases of metabolism; they are further the specificity of proteins. The

*See also Morgan's remarks in his paper quoted in Bib. 8.

†A detailed presentation of the following views will be published as soon as conditions permit..

mechanism of the distribution of the determinants of these characters in the process of heredity is in both cases the same, the distribution by means of the chromosomes. Then, just as the differentiation of sexual characters is influenced by endocrine action, important characters of general organization are influenced by the hormones of thyroid, hypophysis, etc., like growth, correlation of organs, metamorphosis, nervous functions, metabolism and instincts. We feel justified, therefore, in applying the same conceptions to all other processes of heredity which we were able to derive for the case of sex because all the differences occur within the offspring of the same parents. So we conceive of the mechanism and physiology of heredity thus: The fertilized egg furnishes in its protoplasm the chemical material and the physical substratum for the processes of growth and differentiation. The chromosomes furnish the determinants or factors for the specific direction of these processes, which make the offspring similar to the parents. These factors are enzymes, which are not only characteristic in regard to their quality, but which are handed over to the sex-cell in very exact quantities or concentrations. As the reactions accelerated by these enzymes take place with a velocity in proportion to their concentration, a very subtle mechanism is given for the production of definite reactions with a different velocity, thus assuring the always returning rhythm of differentiation. As only certain products of reaction will be influenced by the next working enzyme, localization is possible in addition to rhythm. And the reaction accelerated by the enzymes of heredity to a definite velocity, is the formation of hormones, directing growth, metabo-

lism and differentiation, similar in their action to the known hormones of the thyroid, hypophysis, etc. Thus the entire problem of heredity assumes at a certain point an endocrine aspect.

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BOOK REVIEWS

THE SECRETION OF THE URINE. By Arthur R. Cushny, M.A., M.D., LL.D., Professor of Pharmacology, University College, London. 1917. Pp. 241 with 36 illustrations. New York. Longmans, Green & Co., $3.00 net.

In the words of Cushny, "no other organ of the body has suffered so much from poor work as the kidney and in no other region of Physiology does so much bad coin pass as legal tender." In the preparation of the book some 6000 pages had to be evaluated and the attempt to treat all of this literature in detail is frankly abandoned as impossible in a single monograph. Various papers therefore have been dismissed with scant consideration, whereas those which the author regards as more significant, have been treated at some length. Although the author writes to some extent as a partisan, the ascertained facts in regard to renal physiology are treated apart from his well known theory. The book begins with a study of the anatomy and histology of the kidney, then takes up the constituents of the urine, physical factors in secretion, and the work, gaseous metabolism and blood supply of the kidneys. This is followed by an interesting chapter on the theories of renal secretion. The chapter contains a considerable amount of material which is interesting from the standpoint of secretion in general. In the next section, the evidence bearing upon the functions of the tubules and glomeruli is treated at length. The relation between the blood and the formation of the urine is next taken up. The action of diuretics and other drugs is treated in a short chapter followed by a brief discussion of the subjects of glycosuria and albuminuria, nephritis and renal disorders.

From the standpoint of technical endocrine interest, it is unfortunate that lack of space prevented

any extensive consideration of the action of the hormones on renal function. Much of the work bearing on the relation of pituitary extracts to renal secretion is ignored, the author contenting himself with a brief review of Schaefer and Herring's work and the later paper of Houghton and Merrill. The situation is left with the statement that pituitrin is a diuretic, but whether the diuretic effects are exerted specifically on the renal cells or whether they are brought about by circulatory changes is left undecided. The inadequacy of the evidence offered for the diuretic functions of pituitrin is not brought out. Since Cushny's book went to press, Motzfeldt has shown that the existing evidence, in itself, is inconclusive and that as a matter of fact in normal animals, pituitrin is an anti-diuretic.

The effect of adrenin on the kidneys receives only seven lines which brings out the facts that this drug injected intravenously constricts the renal vessels and arrests the secretion of urine while in subcutaneous injections it increases the sugar of the blood and often causes glycosuria. Marshall and Davis' statement that extirpation of the suprarenal glands tends to impairment of kidney activity is also mentioned, the implication being that this is due to a lack of circulating adrenin. Whether or not adrenin in smaller doses or when slowly absorbed actually does cause constriction of the renal vessels has not been determined. It is possible, if not probable, that small doses intravenously or larger doses subcutaneously actually cause vascular dilatation in the kidney and hence diuresis. The supposition that suprarenal deficiency amounts essentially to adrenin deficiency is, in the light of present day knowledge, quite indefensible.

Despite the inadequacy of the monograph on these endocrine topics, it is one of great medical interest and value, embodying as it does, the well considered conclusions of a master in the field covered.—R. G. H.

VAGOTONIA, H. Eppinger u. L. Hess. Die Vagotonie Eine Klinische Studie. Sammlung klinischer Abhandlungen uber Pathologie und Therapie der Stoffwechsel—und Ernahrungsstorungen. Herausgegeben von V. Noorden 9 and 10, Heft. Berlin, 1910, Hirschwald.

VAGOTONIA: A Clinical Study in Vegetative Neurology, by Dr. Hans Eppinger and Dr. Leo Hess. Authorized translation by Walter M. Kraus, A.M., M.D., and Smith Ely Jelliffe, M.D., Ph.D. Nervous and Mental Disease Monograph Series, No. 20. New York, The Nervous and Mental Disease Pub. Co., 1915.

Although the work of Eppinger and Hess appeared so long ago as the year 1910, the English translation is dated 1915. For this and for other reasons the present seems to be not an inopportune time for a discussion of the "Vagotonia" hypothesis.

It cannot be said that the views of Eppinger and Hess have received any general or widespread acceptance, but there are, in the current literature sporadic references to "autonomin", or "Hormone X", and some few clinical papers in which an attempt is made to explain obscure symptoms or pathological conditions on the basis of the Viennese hypothesis.

To a certain type of mind there is a strange fascination attached to a new long word, especially if it be not particularly cacophonous. The word "vagotonia" is not unpleasant in sound and bids fair to exercise the same kind of soothing effect on the ears of speculative clinicians as "that blessed word Mesopotamia" on the pious old lady in the story.

It will be necessary to state briefly the theory in question. This will be put out in the first instance in the form of an uncritical exposition, the Authors' own words (as they appear in the English translation), being used as far as possible. A discussion of the theory and its physiological foundation follows.

functioning of visceral organs is a well regulated interaction between the two contrarily acting forces.

After a brief account of the anatomy and physiology of the sympathetic and autonomic divisions of the vegetative nervous system, the Authors proceed to lay great stress upon the antagonistic actions of the two, particular reliance being placed upon pharmacodynamical investigations, and especially the pupillary reactions.

Eppinger and Hess restrict the term "autonomic" to the cranial, medullary, and sacral divisions, and employ it in contradistinction to the sympathetic. The word "autonomic" was first used by Langley to apply to all these divisions—the sympathetic and related systems of nerves.

According to Ehrmann, adrenin is continuously flowing from the adrenal bodies, and this exerts a continuous influence upon the sympathetic. "From this it must be concluded that the stimulating effect of the sympathetic upon its end organs is not an intermittent one, only produced when the affected organs become active, but is in reality continuous."

"It is probable that a similar state exists with reference to the autonomic system, and that a specific analogue to adrenalin, an 'autonomin' exists, even though it is not known at present. Substitutes for this are found in certain poisons, pilocarpin and physostigmin. These drugs act exclusively upon the autonomic system."

The Authors believe that "the entire vegetative nervous system is under the control of the glands of internal secretion. Even if the proof of the existence of a hormone for the autonomic system ('autonomin') is not as yet conclusive, yet there is no doubt that there is some substance which exerts a continuous stimulating action upon the autonomic nervous system. It is quite possible that in the central nervous system there exists some common centre which controls the antagonistic actions of these two systems. The normal progress of

Too much activity on the part of one, or too little on the part of the other, will result in either motor or secretory inhibition or stimulation, and may bring about a condition of disease."

The increased tonicity of the autonomic system in man—"vagotonia"—may be diagnosed by the reaction of the patient to pilocarpin. Those who react to 0.01 grm. hypodermically by sweating and salivation will show probably other vagotonic symptoms, such as hyperacidity, eosinophilia, bradycardia, mild arhythmias, particularly respiratory or sluggish bowel action, approaching spastic constipation.

In order to realize the clinical picture of general vagotonia "there must exist a ***vagotonic disposition*** [1] in the patient, that is, an abnormal irritability of all or only a few autonomic nerves which, under the influence of some adequate stimulus . . . may lead to the development of the symptom-complex vagotonia." The Authors give a full description of patients having this "vagotonic disposition." They are "nervous invalids." Among the symptoms are blotchy areas of redness on the skin, excessive perspiration, widening of the palpebral fissures, strabismus, sore throat, diminished respiration, cardiac excitement, etc. Under the head "pathologically increased vagotonia", we have sections devoted to bronchial asthma, vagotonic diseases of the stomach, nervous diseases of the intestines, and cardiac neuroses. Space will not permit any further details as to the pathological and clinical disturbances alleged to be due to "vagotonia."

The starting-point for the whole theory, the foundation of the entire superstructure, is the assumption that, since adrenin acts as a tonic continuous stimulus to the sympathetic system, there must be some substance which performs an analogous

1. The italics are mine.—S. V.

function for the cranial and sacral autonomic fibres. The work of Ehrmann quoted in support of the theory that adrenin serves normally to maintain the tonus of the sympathetic nervous system, was put forward as long ago as the year 1906, and since that time a great deal of work has been carried out upon the physiology of the adrenal bodies. With this work the Viennese Authors seem to be totally unacquainted. Some of it, it is true, has been published since the date of issue of the German version of "Vagotonia." None the less, the view expressed, and repeated in the translation of 1915, must be declared to be years out of date.

It is difficult to adduce any satisfactory evidence that the secretion of the chromaphil tissue is of any service whatever in the normal state of the animal. The discharge of adrenin from the adrenal body is not indispensable for life or health, and there is indeed no reliable evidence that under normal conditions the circulating blood contains any adrenin at all. Space cannot be found here for an extended account of the recent investigations which justify the attitude just indicated, but the reader is referred to an article by the present writer in this Journal Vol. I. pp. 140-152, as well as to the comments thereupon by Professors G. N. Stewart and R. G. Hoskins, and an article by the Editor in the preceding issue of this journal.

If these observations are just, then it follows that the argument for the existence of "autonomin" by analogy with the function of adrenin, falls to the ground. But why should it be necessary to assume that "there is some substance which exerts a continuous stimulating action upon the autonomic nervous system"? Why not make the same assumption for the tonic influence of the spinal cord upon the skeletal nerves? Why not assume that the inhibitory and other influences of the cerebrum upon the lower centres is controlled by a special hormone? As pointed out by Hoskins (l. c.) much confusion has arisen from

the failure to bear in mind that the sympathetic system can of itself do anything that can be accomplished by adrenin. "The adrenals at most merely reinforce the effect of normal sympathetic impulses."

Now if this is the case in respect of adrenin and the sympathetic, what are we to say of "autonomin" and the rest of the autonomic system? Here we have not the excuse of having to find a function for a mysterious powerful drug occurring in the body. The "autonomin" is purely imaginary, and the functions assigned to it can in all probability be carried out perfectly well by the nerve fibres of the "extended vagus."

The work of Eppinger and Hess is called "A Clinical Study", though the amount of actual clinical evidence put forward is remarkably small. The present writer does not venture to deny that some of the pathological disturbances mentioned may be due to an exaggerated activity of certain of the autonomic fibres. It must be confessed, however, that the authors have not proved their case. The chief point of interest for us at present is to determine how far such disturbances are related to the glands of internal secretions and to increased or diminished hormone activity. The reader will have already foreseen what our attitute on this point is likely to be. In the opinion of the present writer the theory as a whole is highly speculative, is based upon a false analogy, and has little or no experimental or clinical evidence in its favour.

The arguments based upon the pharmacodynamics of certain poisons such as pilocarpin and physostigmin, are dangerous. The Authors believe that although nothing is known of their "autonomin", "substitutes for this are found in certain poisons which have been mentioned—pilocarpin and physostigmine. These drugs act exclusively upon the autonomic system." The use of the word "substitute" here is very baffling. It is to be supposed that the Authors mean no more than that there is an

analogy between the activity of their hypothetical hormone and that of certain drugs obtained from plants, and that something may be learned from the mode of action of substances which act selectively on the autonomic system. But readers will be tempted to imagine that the authors actually assume that because certain poisons produce a certain effect in the body, there must necessarily exist in the organism itself a substance having similar actions.

It will be impossible to enter into a detailed discussion of the ingenious attempts of Eppinger and Hess to explain a multitude of symptoms in terms of "vagotonia". We have already seen that individuals who react by sweating and salivation to 0.01 grm. of pilocarpin hydrochloride are stated to be probably vagotonic; and we can readily imagine that on careful search many of such patients will be found to show such symptoms as hyperacidity, respiratory arhythmia or constipation.

Brief reference may be made at this point to some recent contributions to literature by authors who have given their allegiance to the vagotonic theory. Tracy [1] for example, believes that the normal reaction of the skin to stroking is a brief vasodilation followed by a vasoconstriction. The vasodilation is caused by stimuli coming over the autonomic branch of the vegetative nervous system, acting on the hormone x in the blood-stream. The constriction is due to stimuli coming over the sympathetic and acting upon adrenin in the blood. It is stated that status lymphaticus may be diagnosed by the absence of anemic dermography, showing lack of adrenin in the blood-stream [2]. Tracy is of opinion that the conditions known as vagotonia and

1. Tracy, E. A., (a) Boston M. & S. Journ., 1916, clxxv. 197; (b) ibid, 1917, cixxvi, 538.

2. The subject is confused, because there appears to be another sort of "white line" produced by stroking. In this case the line is said to be a sign of adrenal insufficiency. (Sergent, This Jour. Vol. 1, No. 1, p. 18.)

sympathicotonia are due to a hyper-content in the blood-stream of the respective hormones.[1]

The essay of Eppinger and Hess is a glaring example of the one-sided study of the literature which is so common among German and Austrian writers. All the papers quoted are from German journals, and so far as I can determine, most of them are by writers of the Viennese School. Any impartial student of the literature of internal secretion and of the adrenal bodies in particular will hesitate to give the German workers any such prominent position.

An old story tells how once upon a time an international prize was offered for the best essay upon the camel. An Englishman took his gun and journeyed into a far country where camels abound. His essay was rejected. A Frenchman betook himself to the National Library and compiled an account of the animal. His essay was highly commended. A German shut himself in his study and "evolved a camel out of his inner consciousness"—and won the prize. The fable illustrates fairly well the parts played by the three nationalities in the investigations upon internal secretion. The English (and American) workers have made most of the positive discoveries. The French have written lucidly and elegantly upon the subject.[2] The Germans have speculated and theorized till an entanglement of unsupported hypotheses and elaborate imaginings has almost obscured the few fundamental facts at our disposal.

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1. Other recent papers are:—Moltchanow and Lebedeff, "Vagotonus and Sympathicotonus in Scarlet Fever," Roussky Vratch, Petrog. 1916, xv. 457; Smith, I., "Over Activity of Vagus System and Anaphylaxis," J. Nerv. and Ment. Dis. (N. Y.) 1916, xlv, 26.

A very interesting paper has recently appeared on "The Autonomic System as an Integrator, with Special Reference to the Urogenital Organs," Jackson, Surg., Gyn. and Obstet., 1917, xxv, 346. This author justly criticises the pharmacological theories of Eppinger and Hess, but says nothing about "Hormone."

2. The present writer does not wish to underestimate the splendid work of certain of the French investigators. We cannot forget the parts played by Bernard, Brown-Sequard, and in later times, by Gley and his co-workers.

At any rate Eppinger and Hess have "evolved a hormone out of their inner consciousness". We are at present in complete ignorance and we are likely to remain in complete ignorance of any such substance. There is most probably nothing of the kind in existence and in any case we are not warranted in basing any theories, physiological or clinical, upon the evidences put forward.

—SWALE VINCENT.

ENDOCRINOLOGIA PATOLOGIA E CLINICA degli organi a secrezione interna. By Nicola Pende, Professor in Special Pathology in the University of Palermo, Italy. 1916, Pp. 1034 with 147 illustrations, 25 in colors. Milan. Dr. Francesco Vallardi. Lire 35.00. (Paper.)

This is the largest and most comprehensive book on endocrinology that has come to our attention, transcending in size the well recognized monograph of Biedl (while the two volumes of the second German edition of the latter cover 1226 pages, nearly 300 pages are devoted to a bibliography).

In going through Professor Pende's book it is very clear that he has given special study both in the laboratory and in current literature of all countries, and we regret very much that this book has not yet been translated from Italian and hope that an arrangement may eventually be made by which this may be done.

The book is divided into two principal parts, the first devoted to the physio-pathology of the endocrine glands (672 pages) and a second section (340 pages) devoted to clinical consideration.

As we look through this book with our limited knowledge of Italian, we can not refrain from remarking how much work has been done in this phase of medicine by our Italian confreres. In the index of authors alone no less than 650 names of Italian investigators are recorded, and it is not believed that

the work of these ardent students is as appreciated by the profession in this or other English speaking countries as it deserves to be.

To those members of the Association for the Study of the Internal Secretions who are conversant with the Italian language, this book will be of intelligent interest, and we again express the hope that provision eventually may be made for its translation into English or French, and congratulate the author upon his painstaking efforts.—H. R. H.

THE THYROID GLAND IN HEALTH AND DISEASE. By Robert McCarrison, M.D. (R.U.I.), D.Sc. (Belf.), F.R.C.P. (Lond.), Major, Indian Medical Service, Laureat de l'Academie de Medecine, Paris, Member A. S. I. S., etc. 1917. Pp. 286. New York, Wm. Wood & Co. $4.00.

Major McCarrison has made his name famous in medical literature by his ardent application to the problem of the etiology of endemic goiter and he seems to have made out a clear case in favor of the position that at least many goiters are due to bacterial or protozoal infections, and that a generous proportion of these infections are in the alimentary canal.

This new book is divided into three parts, the first (30 pages) dealing with the thyroid and parathyroid glands in health; the second (47 pages) with the factors which cause these glands to depart from health; and the third (162 pages) to the consideration of the morbid states resulting from this departure.

Without a doubt the treatment of goiter by the maintenance of a suitable intestinal antisepsis, as recognized by McCarrison and established by quite a series of clinical experiences in the author's work in the Indian Medical Service, is another important advance in the therapeutics of this disorder. The profession is beginning to realize that focal infections are the subtle causes of several endocrine disorders and

there is plenty of clinical literature establishing the importance of considering disorders of this nature from this standpoint. We believe that a good deal of this trend and investigation has come about as the result of Major McCarrison's numerous contributions to current medical literature, and since this book is the result of many years of experimental as well as clinical investigation, and combines the best in the author's previous papers and addresses, it is of double value to those fortunate enough to have it in their libraries.—H. R. H.

THE INTERNAL SECRETIONS IN PRACTICAL MEDICINE. By Henry R. Harrower, M.D., Fellow of the Royal Society of Medicine (London); Sometime Professor of Clinical Diagnosis, Loyola University, Chicago, Member American Medical Editors Association; Member A. S. I. S., etc. 1917. Pp. 254. Chicago, Chicago Medical Book Co. $2.75.

This book contains a number of addresses and lectures given by the author before various medical organizations and is not, as its title might indicate, a complete survey of the clinical aspects of endocrinology. Among the twenty essays we note several which are of considerable practical interest:

"The Inconspicuous, Everyday Forms of Thyroid Insufficiency" properly directs attention to the frequency of disorders of this character in general practice and since these are so often overlooked its message is of extreme importance.

"The Adrenal Glands and their Significance in General Practice" brings up a subject emphasized previously by such men as Sajous, Sergent and Elliott and considers the matter purely from a clinical standpoint. We may not entirely agree with all the author's deductions. For instance, it is suggested (page 85) that some of the manifestations of malaria are of distinctly adrenal origin—"at one stage in the cycle

of experiences in malaria there is a decided adrenal excitation, due to the sudden periodical liberation of the plasmodia and, of course, their toxins. One encounters the dry mouth as often as salivation, both manifestations of sympathetic stimulation. The heart action is always rapid and sometimes irregular. Then, as an aftermath of the chill, we find the muscular relaxation, prostration, depression and asthenia, all of which are identical with the findings of severe adrenal insufficiency."

Other interesting chapters in which the practical flavor, and hence readability rather than scientific accuracy, is prominent are "The Relation of the Internal Secretions to Neurasthenia in Women," "The Defective Child from the Standpoint of the Internal Secretions," and "The Relation of the Endocrine Glands to Functional Disorders."

THE ORGANS OF INTERNAL SECRETION: their Diseases and Therapeutic Application, A Book for General Practitioners. By Ivo Geikie Cobb, M.D., M.R.C.S., Late Assistant to the Out-Patient Physician, Middlesex Hospital, London; Member A. S. I. S., etc. 1917. Pp. 228. New York, Wm. Wood & Co.

Dr. Cobb contributed a series of articles during 1916 to the Medical Press and Circular, and he has made these a basis of a very practical litle book. The subject is largely considered from the standpoint of therapeutics and hence is more interesting reading to the general practitioner than to the laboratory investigator. As with many contributions to the literature of this subject one finds opportunities to differ with the author and until the endocrine literature is on a much more stable and permanent basis this can not but be the case. To the practical physician whose time is limited, Cobb's book will come as an easy means of getting in touch with the essence of this subject and properly may be called a brief, practical

and altogether readable compendium of clinical endocrinology.

THE ENDOCRINE ORGANS: An Introduction to the Study of Internal Secretion. By Sir Edward A. Schaefer, LL.D., D.Sc., M.D., F.R.S., Professor of Physiology in Edinburgh University; Member A. S. I. S., etc. 1916. Pp. 156. New York, Longmans, Green & Co., $3.50 net.

Some years ago Sir Edward Schaefer delivered the Lane Lectures at Stanford University and as these were of such unusual importance they were published by the University and have lately been republished after having been carefully edited, brought up to date and embellished with numerous figures (there are 104). The author considers his subject from a purely physiological standpoint and his opinions are worthy of great respect for it will be remembered that the profession is indebted to Sir Edward for many advances in our knowledge of the glands of internal secretion. For instance, it was Sir Edward who first announced the fact that the pituitary body was an endocrine organ in 1894-5.

A peculiarity of this book is the author's frequent use of the term autacoid* which he originated and which as yet has not become generally accepted in medical literature.

Sir Edward's book is a carefully conceived and altogether praiseworthy contribution to the permanent literature on this broad subject and we can not but express regret that it contains only 150 pages.—H. R. H.

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*"A specific organic substance formed by the cells of one organ and passed from them into the circulating fluid to produce effects upon other organs similar to those produced by drugs. Such effects are either in the direction of excitation, in which case the endocrine substances producing them are excitatory autacoids and would come under the expression hormones, or in the direction of restraint or inhibition, in which case they are restraining or inhibiting autacoids and would be classed as chalones. The action of an autacoid may therefore be described as hormonic or chalonic, according to the kind of effect it produces."

THE LITERATURE ON THE INTERNAL SECRETIONS

GENERAL SUBJECTS

AUTONOMIC SYSTEM, as an Integrator with Special Reference to the Urogenital Organs. Jackson (H. C.) Surg. Gyn. & Obs. (Chgo.) 1917, xxv, 346.

The autonomic nervous system plays a very important role in the combination of chemical and physical forces upon which rests the physiological state of dynamic equilibrium, so essential for the maintenance of life. It is intimately integrated with chemical correlation through hormones, each system tending to regulate the other. Although the autonomic impulses are in the main independent of volition, nevertheless the effector organs innervated by these fibers can be brought into reaction through reflexes whose centers exist in the central nervous system and whose afferent arcs may originate in the cortical areas. Certain pseudo reflexes (axone reflexes) are possible in this system in contradistinction to the cerebrospinal outflow.

The autonomic system is divided according to the portion of the central nervous system from which the outflow of preganglionic fibers takes place: (a) The cranio-bulbo autonomic tenth, and the eleventh cranial nerves. (b) The thoracicolumbar autonomic covers the outflow between the second dorsal and third lumbar anterior roots. This is ordinarily called the sympathetic system. (c) The sacral autonomic is supplied by the second and third anterior sacral roots.

Considerable importance rests upon the close embryological development of the chromaffin and autonomic systems. Both are developed from the neural crest cells which eventually form the posterior root ganglia. In the lower forms (coelenterates) the former represents the latter as groups of chrome-staining cells placed similar to the sympathetic ganglia. As the autonomic outflow of fibers becomes more pronounced in the higher mammals, the chromaffin system assumes less and less prominence until at present in mammals it is restricted in the main to the medulla of the adrenal bodies. These cells represent post-ganglionic fibers of the sympathetic system. Most of the effector organs innervated by the autonomic outflow receive a dual supply from the thoracico-

lumbar division on the one hand, and the cranio-bulbo or the sacral portion on the other. The effect of the former is antagonistic to the latter.

The state of equilibrium determined by this extrinsic nervous control is dependent upon the ebb and flow of these two antagonistic sets of impulses. There is also distinct evidence of reciprocal innervation in the autonomic system similar to that shown by Sherrington to exist in the cerebrospinal outflow. This mechanism is of exceeding advantage in the automatic filling and emptying of the small and large intestines, the biliary and urinary bladders. The uterus and ureters are also under autonomic control. The hormones and the autonomic system also possess reciprocal control over each other. Stimulation of the cervical sympathetic increases activity of the thyroid and pituitary glands.

Epinephrin exerts a sympatheticomymetic effect through its action on the same peripheral mechanism as the thoracicolumbar autonomic impulse. Pilocarpin reacts similarly upon the cranio-bulbo-sacral autonomic system, but more particularly upon the secretory fibers. This type of substance has been termed vagomymetic since the effects of the vagus as a part of this division of the autonomic are the most prominent and widespread. Acetyl choline was shown by Dale to simulate more closely the general effects of bulbo-sacral stimulation. Atropine removes the effects of vagomymetic substances or prohibits the onset of the effects. A similar paralysant for the sympathetic system has not come to life, unless we consider ergotoxin as fulfilling the conditions.

Attempts have been made to clarify the pathology of the "vegetative" organs, by grouping together as a symptom-complex certain disturbances of the equilibrium in the autonomic system in its widest sense. Some of the symptoms of vagotonia, so called, may be ascribed to an increased activity of the organs or tissues supplied by the bulbo-sacral autonomic; or a similar set of conditions may arise following a decrease in the power of antagonistic impulses flowing over the sympathetics. Patients exhibiting such a syndrome are excessively reactive to pilocarpin. Other abnormal states occur as the result of augmented activity of the sympathetic or a decrease in the strength of the bulbo-sacral autonomic outflow. Such a condition is given the name of sympathetico-tonia. These patients are sensitive to adrenalin and become better after the administering of atropine. Certain methods are in vogue for the determination of vagotonia or sympatheticotonia. Do these clinical pictures represent entities of abnormal functions? What is their value in diagnosis?—Author's Summary.

PLACENTA, regarded as a Gland of Internal Secretion. Frank (R. T.) Surg. & Obs. (Chgo.) 1917, xxv, 329.

The experimental work of the last decade proves that Halban was correct in ascribing to the placenta an action upon the uterus and breasts. Placental extracts (mainly the lipoid fraction) rapidly induce hyperplasia of the uterus and breast (gland tissue and nipples), in castrates or in non-castrated animals. The chemical substance which induces these changes is thermostabile, very resistant to strong alkalies and acids, and completely soluble in 95 per cent alcohol. The substance appears identical in its physical, chemical and biological properties with a similar substance obtained from the corpus luteum. The substance can exert its influence in the absence of the thyroids, adrenals, pancreas, or in the absence of thyroid and adrenals combined. In view of the apparent identity of corpus luteum and placental substance the question arises whether placenta acts merely as a storage reservoir for corpus lutem secretion during the latter half of pregnancy, or whether the placenta elaborates a hormone of its own.—Author's Summary.

SEX GLANDS, Their Relation to Metabolism. Murlin (J. R.) and Bailey (H.) Surg. Gyn. & Obs. (Chgo.) 1917, xxv, 332.

Our results uphold the work of Loewy and Richter so far as the reduction of metabolism after castration is concerned. Removal of the ovaries of our dogs was followed by an increase in weight in both and a lowering of the metabolism in one of 12 to 17 per cent, and in the other of 6 to 14 per cent.

We feel that indirect action has a bearing on this reduction, and we do not believe that the indications point decisively to the loss of a specific stimulus from the ovary affecting the oxidative processes of the cells.

To throw more light on this complex subject, further experiments with animals are necessary.—Author's Summary.

(PARATHYROID, THYROID) Surgical Anatomy of the Thyroid with Special Reference to the Parathyroid Glands. Pool (E. H.) and Falk (H. C.) Ann. Surg. 1916, lxiii, 71.

The variations in the position of the parathyroids in relation to the thyroid are considered. From a study of twenty-five cases the authors conclude that it is advantageous in thyroidectomy to leave in situ the posterior parts of both lateral lobes of the thyroid, thus permitting the recurrent laryngeal nerves and the parathyroids to remain intact in most instances. Complete bilateral extirpation, leaving only the isthmus, should never be considered. The posterior part of one lobe must always be left.—F. A. H.

(UTERUS) Les produits endocrins de l'utérus humain dans les diverses phases de son développement et dans certaines conditions morbeuses spéciales. (Endocrine Products of the Human Uterus in the Different Phases of its Development and in Certain Special Morbid Conditions.) Fornero (A.) Arch. Ital. de Biol. (Pisa) 1917, lxv, 324.

The author describes the appearance of certain lipoid cells in the uterus at different stages of sexual development and at different phases of menstruation. Reasons are given for considering these lipoid cells as an endocrine tissue.

F. A. H.

(THYROID) Sur le contenu en iode de la glande thyréoïde dans les divers âges de la vie et sur les rapports entre le quantitatif d'iode et l'aspect histologique de la glande. (Iodine Content of the Thyroid Gland at Different Ages and the Relations between the Amount of Iodine and the Histological Appearance of the Gland.) Pellegrini (R.) Arch. Ital. de Biol. (Pisa) 1916, lxv, 109.

Iodine was found in the thyroid of three out of thirteen fetuses or newly born children. Among children ranging from eleven days to two years of age, the thyroids of fifteen out of twenty-three contained iodine. The presence of iodine seemed to be independent of the state of nutrition.

From a study of the thyroids taken from one hundred and one adults the author finds the average weight of dry gland to be 3.78 grams. The average amount of iodine was 0.004 grams for the entire gland. The total maximum value of iodine was attained in individuals 45 to 55 years of age (0.007 gram). It decreased rapidly during the next ten years to 0.003 gram.

The variations in iodine content of the thyroid in different morbid conditions are discussed.

Thyroid glands of different histological types are described and their relative iodine content mentioned.—F. A. H.

(PITUITARY, ADRENIN) Does the Pituitary Gland contain Epinephrin or a Compound similar to it? Watanabe (W. K.) and Crawford (A. C.) J. Pharm. and Exper. Ther. (Balt.) 1916, viii, 1.

Certain similarities in the physiological action of extracts of the pituitary gland and of epinephrin have long been known. Watanabe and Crawford point out that there are probably several active compounds in the pituitary gland, one of which has an action much like that of epinephrin. The main argument in favor of this view is that after intravenous injection of ergotoxin into decapitated cats, they produced vasomotor reversal with extracts of pituitary gland, like that

from epinephrin. The color reactions which they obtained from pituitary extracts and which resembled qualitatively those from epinephrin were mostly made with extracts of the pituitary gland made by the method which Weidlein used in extracting epinephrin from the suprarenal glands. These might be due to decomposition products of some amino-acids and not necessarily pre-existing in the glands, but Watanabe and Crawford do not enter into the discussion as to whether the physiological reaction of the pituitary gland extracts, which resemble epinephrin, and the color reactions are due to the same or different compounds. This is to be discussed later. They argue it is the same.

Watanabe and Crawford find that the action of extracts of the pituitary gland can be explained by assuming the presence of a compound resembling epinephrin modified by the presence of a depressor compound.—Author's Abstract.

ENDOCRINE ORGANS, The Eye and. Zentmayer (W.) (Phila.) Jour. A. M. A. (Chgo.) 1917, lxiv, 1.

The author is to be congratulated upon having considered the subject broadly—taking into consideration the relative lack of familiarity of the subject among his listeners. He has summarized the present day information regarding the effect of the secretions of the different glands on the general system with special reference to the effects on the eye. As is to be expected, of course, the thyroid and pituitary are more exhaustively treated because of the greater availability of the literature concerning these glands.

The article is so comprehensive as to bear reading and rereading by those especially who are sufficiently interested to want to apply themselves to observations along similar lines.

One point about which, of course, little has been written is the administration of endocrine substance in the treatment of ocular conditions. The author's proof of his having gone deeply into the subject leads one to hope that he will build on that foundation which he presents, chiefly historic and theoretic, a superstructure of practical organotherapy and give us his findings therefrom in a subsequent article.—R. S. L.

(PITUITARY) On the Relationship between the Hypophysis and Lethargy of Hibernating Animals, with Special Consideration of the Genesis of Lethargy. Salmon (A.) Lo Sperimentale (Florence) 1916, lxx, 345.

The article is an extensive, critical review of the relationship of the hypophysis to sleep, its possible relationship to hibernation and a general discussion of the latter condition. No new data are presented and its value consists in the extensive way in which previous work is reviewed.

The author discusses his theory of sleep based upon the relationship between the disturbance of sleep and changes in the hypophysis; the relation of hypersomnia and insomnia with hypopituitarism and hyperpituitarism. He believes that sleep has its seat in the cortical cells and is associated with the elaboration of a reserve substance for the organic repair of the nerve cells after the intoxication of the waking hours. The action of the hypophysis is due to its antitoxic and trophic property as regards the nerve centers, and consists in protecting the cortical cells from the toxic products of metabolism and caring for their nutrition.

He discusses at length the theory of Cushing and Goetsch on the relationship between the hypophysis and the lethargy of hibernating animals. He finally discards the theory on the following grounds: In hypophyseal disease the torpor never becomes nearly so great as is observed in hibernation; the hibernating animal awakens immediately in response to definite stimuli as changes in temperature; no pathological changes are noted in the nerve cells of hibernating animals as occur in hypophyseal disease; loss of hypophyseal function can not explain the marked hypothermia noted in hibernating animals. However, he believes that pluriglandular insufficiency plays a noteworthy part in the mechanism of lethargy. It should be emphasized that no new data are presented, and that his conclusions against the theory of Cushing and Goetsch are based wholly upon the dissimilarity between hypophyseal disease and hibernation.

He discusses the theories of hibernation in detail and presents his own theory based upon the function of the hibernating glands. Lethargy is the sign of a severe fall of the internal temperature, particularly that of the brain, as a result of which there is a distinct slowing of organic metabolism. The hibernating gland is the only organ which is very active during hibernation. It maintains the negative life of the animal and inhibits the function of all the other organs. In this respect it is a true endocrine gland, and while it is active it inhibits the activity of all other glands of internal secretion.

F. C. M.

(PARATHYROIDS) Tetania Parathyreopriva; its Nature, Cause and Relation to Idiopathic Tetany. Paton (D. N.) and collaborators. Quar. Jour. Exper. Physiol. (Lond.) 1917, x, 203-377.

Part I. Introduction. General methods and symptoms. Paton (D. N.) and Findlay (L.).

Idiopathic tetany and the various theories regarding its etiology are considered.

The previous work upon experimental tetany is dealt with in the three periods:

(a) Before the recognition of the possible significance of the parathyroid;
(b) While the distinction between the thyroids and parathyroids was still doubtful;
(c) After the direct implication of the parathyroids in the production of the symptoms had been established.

The evidence that the condition is a true tetania parathyreopriva is considered to be conclusive.

The method of removing the parathyroids is discussed, and the authors infer that it is impossible to get rid of the internal parathyroids with certainty by any operation but complete thyroparathyroidectomy. The existence of supplementary parathyroid tissue in about 50 per cent of cats and in probably about 5 per cent of dogs is shown to explain the absence of symptoms in some cases of thyroparathyroidectomy.

The symptoms of tetania parathyreopriva are summarized and some of the factors modifying the character and onset of the symptoms are briefly considered.

Part II. The parts of the central nervous system involved. Paton (D. N.), Findlay (L.) and Watson (A.).

The authors conclude that the nervous symptoms are due to the condition of the central nervous system.

In the production of the spasticity, tremors and jerkings the cerebral arc is not directly involved. The increased violence of these symptoms after decerebration is due to unopposed action of cerebellar and spinal arcs.

The tremors and jerkings develop independently of the cerebellar arc, but the integrity of this arc is essential for the production of the sustained spastic tone.

The integrity of the spinal arc is not essential for the development of the tremors and jerkings, since they persist after section of the dorsal roots of the spinal nerves. The efferent neurones are the structures primarily implicated.

In advanced cases of tetania parathyreopriva disturbances of equilibrium seem to indicate a secondary involvement of the cerebellum.

In such advanced cases the onset of epileptoform convulsions probably indicate the secondary involvement of the motor part of the cortex cerebri.

Part III. The changes in the peripheral nerves and in the muscles. Paton (D. N.), Findlay (L.) and Watson (A.).

Any marked decrease in the amount of parathyroid tissue is followed by a very marked increase in the electrical excitability of the peripheral motor nerves. The same is found in all cases of idiopathic tetany.

As a rule no alteration of the normal sequence of the various responses results.

Mechanical excitability, so characteristic of idiopathic tetany, does not appear to be such a prominent feature of tetania parathyreopriva.

The increased electrical excitability of the peripheral nerve is independent of changes in the central nervous system. It occurs after section of the nerve and persists until degeneration sets in; whether the nerve be cut before, with or after the removal of the parathyroids.

The electrical excitability of muscle to direct stimulation is increased after parathyroidectomy, although not generally to the same extent as that of the nerve.

This is chiefly due to an increased electrical excitability of the neural structures in the muscle, since it is generally abolished by a dose of curare sufficient to block nervous impulses and the increased excitability of the muscles decreases as the nerve degenerates after section. In some cases there is evidence of increased excitability of a post-neural substance.

The nerve-ending is the part of the neural element which is acted upon, since in cross-circulation experiments the result of stimulation of the sciatic nerve bathed in the animal's own blood varies with the changes produced in the peripheral nerve supplied with foreign blood.

In tetania parathyreopriva the increased electrical excitability of the peripheral motor neurone is not proportional to the intensity of the symptoms due to the conditions of the central nervous system and after a definite fit it may be markedly reduced. In idiopathic tetany the relation is somewhat closer, but is not directly proportionate.

Hence increased electrical excitability can not be regarded as a measure of the severity of the condition.

Part IV. The etiology of the condition and its relationship to guanidin and methyl-guanidin intoxication. Paton (D. N.) and Findlay (L.).

The authors conclude that there is no direct interrelationship between the parathyroids and the thyroids.

There is no evidence that the parathyroids exercise a direct controlling influence on the central nervous system.

The symptoms of tetania parathyreopriva are not primarily due to decrease in any constituent of the body, e. g. calcium ions.

The symptoms are not due to an increase in ammonia or xanthin or iminazolylethylamin in the blood.

The symptoms are identical with those produced by the administration of salts of guanidin and methyl-guanidin.

Part V. Guanidin and methyl-guanidin in the blood and urine in tetania parathyreopriva and in the urine in idiopathic tetany. Burns (D.) and Sharpe (J. E.).

The analytical results are summarized as follows:

Guanidin (and the methyl-guanidins expressed as guanidin) in mg. per 1000cc.

A. Blood. Dogs—Normal (average of 5), 1.0. Parathyroidectomy (average of 8), 8.7.

B. Urine. Dogs—0.25 (average of 6). 1.1 (average of 6). Children—Average of 5 (8 analyses). Idiopathic tetany (average of 3 cases; 13 analyses). Active tetany, 0.58. Latent tetany, 0.38. Recovering from tetany, 0.12.

The authors infer that there is a marked increase in the amount of guanidin and methyl-guanidin in the blood of dogs after parathyroidectomy and in the urine of children suffering from idiopathic tetany.

Part VI. The action of the blood-serum of animals in tetania parathyreopriva on the skeletal muscles of the frog. Wishart (G. M.).

In certain cases the serum of parathyroidectomized dogs acts upon the muscles of the frog in the same way as do dilute solutions of guanidin and methyl-guanidin. But the variations in the susceptibility of the muscles of different frogs renders this biological test unreliable.

Part VII. A comparison of the influence on the protein metabolism of parathyroidectomy and the administration of guanidin. Burns (D. A.).

After the administration of guanidin hydrochloride to dogs the excretion of nitrogen was increased immediately and out of all proportion to the dose. The ratio of urea nitrogen to total nitrogen was decreased. The proportion of the total urinary nitrogen excreted in the form of ammonia showed a slight decrease in feeding animals and generally a slight increase in fasting animals.

The excretion of creatin was only slightly if at all increased, but the percentage of unidentified nitrogen rose markedly immediately after the injection of guanidin.

From the close similarity of these effects to those resulting from parathyroidectomy in dogs, the author concludes that the two states are probably identical.

Part VIII. The functions of the parathyroids and the relationship of tetania parathyreopriva to idiopathic tetany. Paton (D. N.) and Findlay (D.).

Summarizing the results of their investigations, the authors conclude:

A. The parathyroids regulate the metabolism of guanidin in the body. By doing so they probably exercise a controlling influence on the tone of the muscles.

B. Tetania parathyreopriva and idiopathic tetany are identical as regards their character and metabolism, and, although the histological evidence is not conclusive, in all probability the parathyroids are implicated in the latter as in the former.—T. B. R.

The Preparation and Standardization of Ovarian and Placental Extracts. Morley (W. H.) Surg., Gyn. and Obs. 1917, xxx, 324.

Morley gives due emphasis in his article to the need for more uniform methods in the preparation of ovarian and placental extracts. Tangible laboratory and clinical data are still moreover lacking in extent. A review of the more important articles on the above subject reveals the circumstances that it is only within the last ten years that an attempt has been made to isolate the active principle of the ovary and placenta, especially the former. Iscovenso (1908) obtained "lipoids" from the red blood corpuscles, hypophysis, kidney, adrenals, ovaries, the testicles and the corpora lutea, and discovered they exerted a certain action on the female genitalia. The "homo-stimulating" lipoids, he found, had an action on the same organ from which they were derived, the "hetero-stimulating" lipoids exercising an action on different organs—this division he discovered later being purely arbitrary. Hermann (1915) believes he has succeeded in separating the "active substance" of the corpus luteum and of the placenta as a specific chemical substance, having identical physiological properties. Hermann possibly obtained his so-called active substance in a purer state. After engaging in special research work along this line during the last two years, Morley expresses the opinion that up to the present time no ideal method of preparation has been formulated, and until that is accomplished, standardization of the product will not be attempted. Considering the newness of the subject, the article concludes with quite an extensive bibliography.—Author's Abstract.

(THYMUS) Sull 'anatomia patologica e normale del timo nei lattanti. Vassiutotschkin Charkowski. La Pediatra, 1917, xxv, 433.

The thymus from birth to the twelfth month increases in weight from 7 to 12 gm. In some cases of general atrophy the thymus is larger as if to compensate for the loss. The gland is heavier in males. Degeneration is brought about by insufficient alimentation. Hereditary syphilis causes atrophy of

the thymus. Diseases of the respiratory tract, if not tubercular, do not interfere with the development of the thymus; but there is usually hyperplasia in gastro-enteric diseases. while tuberculosis and diphtheria both cause degeneration.—G. V.

(INTERNAL SECRETIONS) Lipodystrophia Progressiva: Weber (F. P.), Brit. J. Chil. Dis. 1917, xiv, 81.

The author makes an exhaustive study of the literature on this rare condition and concludes as follows:

1. That lipodystrophia progressiva is not always progressive, certainly not in regard to the extent of the area affected.

2. That it usually commences in childhood at 6 or 8 years of age.

3. That in some cases, the fat atrophy in the upper parts was preceded by increase of fat in the buttocks or legs; this increase of fat was, therefore, apparently the first sign of the commencement of the disease or syndrome in question.

4. That this disease or syndrome is not confined, as at first it was supposed, to the female sex. Genuine examples have been recently recorded in males, and it is probable that some of the cases, especially in males, which were formerly labeled "bilateral facial atrophy" were likewise genuine, though less extensive examples of lipodistrophia progressiva. Perhaps it will be found that, in males, the fat atrophy is more often limited to the face and neck, than in females.

5. That the etiology is unknown, but is probably connected with a disorder of the internal secretions.

6. That the fat atrophy, however disfiguring it may be, and though it may give rise to annoying suspicions of tuberculosis, etc., does not signify any danger to life, and is not usually accompanied by loss of strength or general health.—M. B. G.

EXPERIMENTAL INVESTIGATION

(SPLEEN) Beitrage zur Physiologie der Drusen. 24 Mitteilung. Fortgesetzte Beitrage zur Lehre von der Funktion der Milz. Das Zusammenwirken von Leber und Milz. Asher (L.) and Ebnother (G.) Biochem. Zeitschr. (Berlin) 1916, lxxii, 416.

Spleen-extract by itself has practically no hemolytic action. Liver-extract by itself has a definite hemolytic action of varying magnitude. A mixture of the two extracts has a much more intense hemolytic action than liver-extract by itself. The activating substance in spleen-extract is destroyed by heat. Spleen-extract in physiological salt solution has a slight power of decomposing hemoglobin. Liver-extract has a somewhat greater power of decomposing hemoglobin. A mixture of the two destroys hemoglobin more rapidly than either alone. This substance in spleen-extract is heat resistant and is not a lipoid. A new function of the spleen is thus demonstrated, namely, that of supplying substances which activate the functions of the liver.—T. B. R.

(TESTIS) The Effects of Testicular Transplants upon Vasomotor Irritability. Wheelon (H.) and Shipley (J. L.) Am. Jour. Physiol. (Balt.) 1916, xxxix, 394-99.

The article deals with the relationship between the sympathetic nervous system and the internal secretions of the testis. Vasomotor reaction to intravenous injections of nicotin was taken as the criterion of the activity of the sympathetic system. Nicotin was used because of its selective action upon the sympathetic ganglia and the vasomotor centers proper.

Responses of the vascular system to nicotin gave evidence that one of the effects of castration is to depress the activity of the sympathetic system. From six to eight weeks after castration pressure responses to nicotin averaged 50 per cent. lower than reactions to the same dosage before removal of the gonads. Readings made from 10 to 22 days after the reception of a testicular transplant demonstrated a rise of 55 per cent in the activity of the vasomotor mechanism, or a return to 77 per cent of the normal. The transplants were found to remain active for at least 22 days. Castration and subsequent transplantation of testicular tissues caused but slight change in blood pressure. The series of dogs gained 5 per cent in weight during the period after castration.

The findings point to the conclusion that a direct relationship exists between the sympathetic nervous system and the primary reproductive organs. Castration results in a depres-

sion of the sympathetic mechanism, while the re-establishment of the lost parts partially reinstates normal activity.

Normal dogs which gave a feeble nicotin reaction subsequently proved unusually susceptible to infection.—Authors' Abstract.

(PANCREAS) The Absorption of Fat in Partially and in Completely Depancreatized Dogs. McClure (C. W.), Vincent (B.) and Pratt (J. H.) Jour. Exp. Med. (N. Y.) 1917, xxv, 381.

Recently McClure, Vincent and Pratt of the Harvard Medical School have made investigations concerning the possible control of fat absorption from the intestines in dogs by means of an internal secretion of the pancreas. In 1856 Claude Bernard presented detailed evidence to show that the external secretion of the pancreas is of great importance in the process of digestion and in the absorption of fat from the intestines. His findings were not accepted by the physiologists of that time. Since then most of the investigators of the subject have been unable to confirm Bernard's results. In 1905 Lombroso working with dogs found that a large percentage of fat was absorbed after all direct communication between the pancreas and duodenum was supposed to have been removed. This was also true if the pancreas was extirpated except for a small portion which discharged its juice through a permanent fistula in the abdominal wall. When complete depancreatization had been effected there was either slight or no absorption of fat. He concluded that the absorption is governed by an internal secretion of the pancreas. Fleckseder and Jansen confirmed these findings. McClure, Vincent and Pratt found (1) that the absorption of fat was always markedly disturbed by the exclusion of pancreatic secretion from the intestines; (2) that after the complete removal of all pancreatic tissue from an animal, the absorption of considerable amounts of fat can still take place, and (3) that dogs with a subcutaneous transplant secreting and discharging juice externally absorbed no more fat than dogs in which the pancreatic remnant was undergoing rapid atrophy and sclerosis. Hence, the condition of the pancreatic tissue remaining in the body does not influence the amount of fat absorbed by the intestine. From these findings the authors conclude that there is no evidence that fat absorption from the intestines is governed by an internal secretion of the pancreas.—Authors' Abstract.

(THYROID) Quelques resultats de la methode de cultures de tissues. V La glande thyroide. (Some Results from the Tissue Culture Method. V The Thyroid Gland.) Champy (C.) Arch. d. Zool. Exp. et Gen. (Paris) 1915, lv, 61.

In tissue cultures of adult thyroid of rabbits and dogs the colloid is rapidly absorbed, the cytoplasm of the epithelium becomes quite granular. After about 24 hours the cells of the vesicles multiply and the lumen is obliterated and the vesicles are transformed into nodules. The epithelial cyptoplasmic granules are large and resemble colloid. After 48 hours the tissue resembles parathyroid rather than thyroid in appearance. The epithelium in the center of the culture may be completely destroyed through asphyxiation, but at the periphery normal mitosis may be seen. The epithelium proliferates rapidly, and after about four days it is difficult to distinguish the different elements of the culture. The epithelial cells tend to inhibit the growth of connective tissue in the cultures. At the periphery of the culture vesicles may form. —E. R. H.

ADRENALIN and Pituitrin, On Antagonism and Synergism of. Vershinin (N. V.) Publications of Imperial University (Tomsk) 1916, lxiv.

Experiments were made on the isolated frog heart (Williams' method). The drugs were either perfused through it, or the heart was placed into the solutions. Adrenalin and pituitrin are physiological antagonists with regard to their action upon the heart. The functional state of the cardiac nervous system is of great importance (experiments under atropine and chloral-hydrate). It follows that the above mentioned drugs do not act on each other physically or chemically, but there is a pure physiological process, adrenalin acting on the sympathetic fibers, pituitrin on the peripheral inhibitory system of the heart.—Physiol. Abstr.

(PITUITARY) The Appearance of the Pressor Substance in the Fetal Hypophysis. Lewis (D.) Jour. Exp. Med. (N. Y.) 1916, xxiii, 677-681.

Extracts of the entire gland were used in this work as separation of the anterior and posterior lobes is impossible at the age when the pressor reaction is first obtained.

Extracts of the hypophysis of fetal pigs measuring from 275 to 285 mm. (crown-coccyx measurement) gave a decided pressor effect. Intravenous injection of 0.05 gm. of dried hypophyses from fetal pigs measuring 175 mm. extracted in 5 cc. of normal salt solution gave a decided pressor effect, such as is usually obtained by the intravenous injection of extracts made from adult glands. Intravenous injections of saline extracts of hypophyses from fetal pigs measuring 125 mm. gave different results. In some cases a slight pressor effect following a primary fall was observed, while in other instances no change in the tracing was noted.

From these studies it seems probable that the active principle of the pars intermedia, using the pressor substance as an index, begins to appear in fetal pigs measuring 125 mm. or slightly more. As far as can be estimated a fetal pig measuring 125 mm. is about nine and one-half or ten weeks old from conception. During the period represented by the differences between 125 and 175 mm. the secretion of the pars intermedia becomes as active as that of the adult gland.

In the glands of the ages above mentioned there are no traces of the hyaline bodies described by Herring, but the pars intermedia is physiologically active.—Author's Abstract.

(ADRENIN) Note on Vagus Stimulation of the Adrenalised Heart. Kuroda (M.) and Kuno (Y.) Jour. Physiol. (Lond.) 1915, l, 154.

The experiments reported indicate that the inexcitability of the cardiac vagus after injection of adrenin is due to its direct action rather than to an increase in intracardiac pressure.

Small amounts of adrenin were ineffective, larger amounts (0.07 to 0.1 mg.) abolished vagus response. In the "heart-lung preparation" the vagus did not recover from adrenin while such effects were only temporary in the intact animal. Moreover in the latter the amount of adrenin necessary to abolish the action of the cardiac vagus was less than that required to double the blood pressure.—F. A. H.

(ADRENIN) Evidence that the Active Principle of the Retroperitoneal Chromaphil Tissue has the Same Physiological Action as the Active Principle of the Suprarenal Gland. Fulk (M. E.) and Macleod (J. J. R.) Am. Journ. Physiol. (Balt.) 1916, xl, 21.

Inhibition of intestinal contraction and augmentation of contraction in the virgin uterus were taken as evidence of the presence of adrenin. Acid extracts of the retroperitoneal chromaphil tissue of man, dog, cat, rabbit, guinea pig, white rat, calf, sheep and pig gave positive evidence of adrenin. Extracts of the sympathetic ganglia and of the epididymis of the dog gave negative results.—F. A. H.

(THYROID, PITUITARY) Morphogenetic Changes in the Pancreas Produced by Thyroid and Pituitary Feeding. Kojima (M.) Jour. Physiol. (Lond.) 1916, l, xlv.

The addition of thyroid or boiled thyroid extract to the food of rats causes increased growth of the pancreas. In a few days the cells multiply and become smaller, the zymogen diminishing. After two or three weeks the multiplication ceases, zymogen accumulates and the cells increase in size.

Feeding of posterior lobe of pituitary body (anterior lobe has no effect) causes vacuolization of the cells, accompanied by edema of the whole organ excepting the islets of Langerhans. There is an accumulation of granules in the cells of the latter. Edema is also produced in the liver and testicle.

F. A. H.

(ADRENAL) The Liberation of Epinephrin from the Adrenal Glands by Stimulation of the Splanchnic Nerves and by Massage. Stewart (G. N.), Rogoff (J. M.) and Gibson (F. S.) Jour. Pharm. and Exp. Ther. (Balt.) 1916, viii, 205.

The authors employed cats and dogs, one eye of which had been denervated by removal of a superior cervical ganglion several days before. It was found that stimulation of the splanchnic nerves causes dilatation of the pupil of the denervated eye provided the blood is allowed to flow from the adrenals to the eye. Slowing of the circulation increases the time between the beginning of the stimulation and the response. A belated response occurs even with the carotids clamped provided a longer or stronger stimulus is used. The latent period of the eye response obtained by injection of adrenin into the renal vein or the femoral vein was about equal to that after the stimulation of the splanchnic nerve, showing that the latent period for the liberation of adrenin from the adrenal is short (a fraction of a second). Latent periods are given under various conditions. The amount of response increases up to a certain point with the duration of the stimulation.

Massage of the adrenals produces an eye response even after splanchnic stimulation ceases to be effective. Massage reaction is soon exhausted.

Previous fright or administration of morphine to cats did not render exhaustion of the adrenals, by splanchnic stimulation, easier.

An interesting fact was the great number of successful eye responses obtained from a single gland of a cat weighing 1.5 kg. In one case fifty responses which, according to the amount of adrenin necessary to evoke similar responses, would require a total of 0.4 mg. Judging from the amount of adrenin found in adrenals by assay (Elliott, Jour. Physiol. 1912, xliv, 374) it seems improbable that all could have come from the initial store.—F. A. H.

(TESTES) Histological Changes in Testes following Vasectomy. Myers (B. D.) Anat. Rec. (Phila.) 1916, x, 228.

In albino rats ninety days after vasectomy degenerative changes in the seminiferous tubules was observed, but the interstitial cells, which are believed to produce an internal secretion, were not affected by the operation. After 120 days

the seminiferous tubules were almost completely disintegrated, but the interstitial cells still remained intact. The author concludes that vasectomy brings about sterilization without disturbing the secondary sex characters or the psychic life.—E. R. H.

The Effect of Adult Chicken Organ Grafts on the Chick Embryo. Murphy (J. B.) Jour. Exp. Med. (N. Y.) 1916, xxiv, 1.

Bits of spleen, liver, kidney and bone marrow of adult chickens, when grafted on to the membranes of growing chick embryos, caused certain changes in various organs of the embryo. The membranes contained small nodules of developing leucocytes. The spleen was enlarged and hemorrhagic or congested, and in the stage of developing blood cells was advanced. The skin and subcutaneous tissues also contained developing blood cells. Similar nodules occurred within the liver and kidneys.—E. R. H.

(CORPUS LUTEUM) Heredity and Internal Secretions in the Origin of Cancer in Mice. Loeb (L.) Am. Jour. Physiol. (Balt.) 1916, xl, 127.

In earlier investigations the author found that a combination of a mechanical stimulus and the influence of a substance secreted by the corpus luteum led to the production of rapidly growing tumor-like formations. These facts suggested the possible importance of corpus luteum for the spontaneous development of cancer in mice.

Castration of mice at six months of age or less diminished the cancer incidence from 60 or 70 per cent to 9.9 per cent. Non-breeding mice with functional ovaries developed cancer in a smaller percentage of cases and at a higher age than normal breeding mice. Castration eliminates the effect of the corpora lutea; non-breeding diminishes or modifies them.

F. A. H.

PANCREAS and ADRENALS, Relation Between. Kamo (K.) Kyoto Igaku Zasshi, iii, 1.

Pancreatectomized dogs were studied, using as controls dogs which had been subjected to operations of equal severity and involving the same loss of blood. Blood was taken from the suprarenal veins by the method of Ehrmann and O'Connor; and its adrenalin content was determined on the ear of a dog by Pissemiski's method. "The blood in the suprarenal veins contained less adrenalin after pancreatectomy than before, thus indicating the absence of any restraining action the pancreas had been said to exert upon the suprarenals, but

rather indicating that the functional loss of one depresses the action of the other."—Chem. Abstr.

PROSTATE, The Lipoid Pigment in, with Special Reference to the Pigment of the Ejaculatory Duct and Prostatic Musculature. Ishihara (M.) Tokyo Igakkwai Zasshi, xxx, 1.

After puberty, under physiological conditions, pigment bodies are present in the glandular epithelium of the prostate, usually in the basal part of the cells near the nucleus. The number and size of the granules correspond to the age of the person. The granules are fine or coarse, irregular, angular masses, with a peculiar yellow or yellowish brown color; they are not doubly refractive, are gradually decolorized by bleaching solutions, are soluble with difficulty in fat solvents, are unchanged by acids and alkalies, are stained orange red by Sudan III and scarlet-red, purplish by Nile blue, and brownish black by osmic acid, and may also be stained by the method of Ciaccio, Smith-Dietrich and Fischler; they probably contain phosphatides, cerebrosides, soaps, pigment, modified by fatty acids, and cholesterol mixed with fat. Their appearance in the prostatic secretion is evidence of the destruction of granule-bearing epithelium and liberation of the granules, which are not an integral part of the secretion. The pigment granules in the epithelial cells of the ejaculatory duct consist of degeneration pigment, with the same significance as that of the seminal vesicles; the number and size of these granules correspond well with the age. Two kinds of pigment bodies occur in the physiologically pigmented smooth muscle fibers of the prostatic musculature; one class of pigment body is found as very fine, brown granules, giving a faint reaction for fat; the other class of pigment body is characterized by a distinct reaction for fat and a faint reaction for iron.—Chem. Abstr.

(ADRENIN) Researches on the Perfused Heart. Burridge (W.) Quart. Jour. Med. (Lond.) 1917, x, 157.

Adrenin has a two-fold action on the frog's heart; a primary depressing action resembling inhibition, and an augmenting or sympathomometic action. Three factors are concerned in the depressing action of adrenin: (1) The concentration of the drug; (2) the concentration of calcium in the perfusing solution, and (3) the condition of the heart at the time of the experiment. The relations between adrenin and calcium are found to be four-fold and depend upon: the concentration of adrenin, the concentration of calcium, the state of the heart induced by the adrenin and the state of the heart induced by the calcium. Evidence is given that traces of

adrenin render balance between the constituents of an inorganic saline solution of secondary importance in regard to their suitability as media for the maifestation of cardiac activity. The behavior of a heart perfused with a well-balanced Ringer solution never approximates to the behavior of the blood-containing heart, and the change takes place immediately after one solution replaces the other. Unbalanced Ringer solutions, i.e., those containing too much calcium, too little calcium or a considerable amount of potassium, interfered with cardiac activity. Traces of adrenin rendered these unbalanced solutions capable of maintaining cardiac activity and of preserving in great measure the resemblances between the behavior of the heart perfused with them and of the heart containing blood. On the basis of these experiments it is suggested that the proportions between the inorganic constituents of the blood are such as to render it an unsuitable medium for the manifestation of cardiac activity except in the presence of adrenin. The origin of certain symptoms of Addison's disease is traced to such lack of balance. Numerous plates and references are given.—Chem. Abstr.

PARATHYROID GLAND, its Physiological and Pathological Importance from the Experimental Aspect. Voegtlin (C.) Surg. Gyn. & Obs. (Chgo.) 1917, xxv, 244.

The parathyroid gland has a definite physiological function which is still incompletely understood. The presence of a minimum of parathyroid tissue in the body is essential for life and the continuation of normal metabolism. Parathyroid insufficiency seems to be characterized by an increased irritability of the nervous system to the galvanic current, which may be due to the withdrawal of the calcium salts from the blood and tissues. Parathyroid insufficiency leads to an alkalosis which is converted into an acidosis as a result of active tetany. Definite metabolic changes take place in animals after complete parathyroidectomy. Pregnancy puts an extra strain on the functions of the parathyroid, as evidenced by tetany during this period in partially parathyroidectomized animals. Tetany has been observed during lactation in animals with parathyroid insufficiency. Interruption of lactation was followed by recovery. The offspring of partially parathyroidectomized animals exhibit a marked increase in nerve irritability. An intravenous injection of soluble calcium or strontium salts or hydrochloric acid almost instantly removes the symptoms of tetany. However, tetany may reappear after this treatment and the life of such animals can not be saved by the continuous administration of calcium. The administration of parathyroid extract seems to have a temporary cura-

tive effect on tetany animals. Iso-transplantation of parathyroids into animals with parathyroid insufficiency is usually successful. The spontaneous recovery from tetany in experimental animals is probably due to changes in their metabolism (acidosis) caused by the hyperactivity of the skeletal muscles during tetany. The experimental facts do not support the theory that eclampsia is due to hypo-parathyroidism. A condition which might justly be termed hyper-parathyroidism is unknown at the present time.—Author's Summary.

(LIVER) Effect of the Emotions on the Catalase Content of the Liver. Burge (W. E.) and Burge (E. L.) Am. Jour. Physiol. (Balt.) 1917, xliv, 75.

Burge has shown that when there is an increased oxidation the catalase content of muscle is increased, and vice versa. "The object of the present investigation was to determine the effect of stress and combat, where extreme muscular effort is put forth by the animal, on the catalase content of the different organs and tissues of the body with the hope of determining if catalase is formed in situ in the tissues or if it is formed by a particular organ and given off to the blood." In this paper special attention is given to the liver.

Ten young cats from one home, living under the same conditions were used. Five of these cats were placed in a wire cage and a dog with a particular dislike for cats allowed to bark and bite at them for one hour on two consecutive days. At the end of the frightening process on the second day, the cats were killed, and the vessels of the liver washed out with 0.9 per cent NaCl solution until they were free from blood. The livers were then removed, ground up and strained. The amount of oxygen liberated from hydrogen peroxide by one gram of this material, in ten minutes, reduced to standard atmospheric pressure, gave the catalase content of one gram of liver. The other five cats were used as controls.

It was found that the catalase increased by about 90 per cent in the livers of the "fighting" cats, as compared with the normal ones. "This catalase is given off to the blood and is carried to the tissues to be used presumably in producing increased oxidation."—T. C. B.

(This paper derives its endocrine interest from the supposition that emotional stress results in augmented activity of the adrenal and thyroid glands.—Ed.)

(ADRENIN) Effect of Adrenalin on Muscular Fatigue. Gruber (C. M.) Am. Jour. Physiol. (Balt.) 1917, xliii, 530.

Recently Hoskins, Gunning and Berry have shown that adrenin produces active vasodilatation in muscle, and they

think this is the cause of the betterment of muscular contraction which Gruber found to follow the administration of this substance. The present work has been carefully planned to show that adrenin has an action on muscle tissue apart from the improvement in its circulation.

"In the fatigued unaltered nerve-muscle adrenin may increase the height of muscular contraction by a two-fold action, by improvement in the blood supply (vasodilation) and by its chemical action upon some substances in the muscle."

Since adrenin does not better the circulation in a muscle in which the nerve is cut and stimulated, its action in improving the contraction must be due to its chemical action alone. This chemical action may be one or all of the three following processes which are accelerated by adrenin:

1. Conversion of glycogen into sugar.
2. Reconversion of lactic acid into sugar (transformation of fatigue products).
3. The oxidizing of lactic acid into carbon dioxide and water (destruction of fatigue products). T. C. B.

(SALIVARY GLANDS) Contributions to the Physiology of the Stomach. XLI. The Alleged Influence of the Removal of the Salivary Glands on the Secretion of Gastric Juice. Swanson (A. M.) Am. Jour. Physiol. (Balt.) 1917, xliii, 205.

The presence of a secretogogue in the salivary glands has been both affirmed and denied, and Swanson's problem was to decide the point if possible. Dogs with a Pavlov pouch were used. After recovery from the operation the gastric secretion was measured at hourly intervals for six to eight hours, beginning one hour before feeding a standard meal of lean meat, and the observations were continued for from seven to ten days. A curve of normal secretion was thus obtained for comparison, after which the salivary glands were removed and the observations repeated.

Swanson finds that neither the rate of secretion nor the quantity of the gastric juice is altered by removal of the salivary glands. The peptic concentration, as determined by Mett's tubes was also unaffected. There was a distinct rise in the acidity of the gastric juice, but this can be accounted for by the absence of alkaline saliva. The conclusion is that there is no hormone in the salivary glands stimulating the secretion of gastric juice.

In describing the condition of the dogs after operation, the author says (p. 209) that their mouths did not appear as dry as would be expected, and also that their sense of taste did not appear to be altered. Later, in his conclusions, he

accounts for a slight retardation in the maximum secretion rate after a meal by the "decreased psychic secretion owing to the dryness of the mouth and consequent impaired taste." —T. C. B.

ADRENIN. The Effects of, on the Distribution of the Blood. IV. Effect of Massive Doses on the Outflow from Muscle. Gunning (R. E. L.) Am. Jour. Physiol. (Balt.) 1917, xliii, 395.

Small doses of adrenin were used, and the amount gradually increased. When the dosage reaches 1 or 2 cc of a 1:1000 solution the pure dilatation changes to constriction as evidenced by a diminished venous outflow. After return to normal there is a tendency to "over recovery" shown by an increase in the rate of outflow. This "over recovery" is probably due to fatigue of the vascular musculature.

The threshold for vasoconstriction varies. Prolongation of the experiment tends to lower the threshold. Increase of concentration has the same effect. For example, 5 cc of a 1:5000 might produce local dilatation without blood pressure reaction, whereas 1 cc of a 1:1000 would cause vasoconstriction.—T. C. B.

(ADRENALS) The Vascularity of the Adrenal Bodies. Burton-Opitz (R.) and Edwards (D. J.) Am. Jour. Physiol. (Balt.) 1917, xliii, 408.

Burton-Opitz's recording stromuhr was inserted into the suprarenal vein of large dogs, and it was found that a gland weighing 1.72 grams (average) receives 0.142 cc of blood per second or 8.5 cc per minute. At a pressure of 100 mm. Hg. 100 grams of gland receives 490 cc per minute. Compared with his figures for other organs, the suprarenals are exceeded in vascularity only by the thyroid.

The question of splanchnic stimulation is also discussed, and some doubt is expressed as to the existence of a dilator mechanism in the adrenals.—T. C. B.

SECRETIN, Influence of, on the Number of Erythrocytes in the Circulating Blood. Downs (A. W.) and Eddy (N. B.) Am. Jour. Physiol. (Balt.) 1917, xliii, 415.

Beveridge and Williams claim to have observed an increase in the number of red corpuscles after the administration of secretin. Their proteomorphic theory of immunity depends upon the power of the red cells to hydrolyze proteins. If this be correct, any agent which increases the red cells is of therapeutic value. Such an agent, however, to be efficient, should not only produce, but also maintain, a largely increased

erythrocyte count. These ideas led the authors to try the effect of arbitrarily fixed doses of secretin when given intravenously, and also the effect of the same dose when given hypodermically.

They prepared secretin from dog's intestines, and rabbits were used for the experiments. The results of a long series of experiments show that it is possible to produce a considerable increase in the red corpuscle count per cubic millimeter by administering secretin. The effect appears quickly, but is transient. Repetition of the dose at short intervals may prolong the increase, but it promptly drops after the last dose. Daily doses over a period of five days have no lasting effect on the red count. The most efficient dose was found to be 1 cc per kilo of body weight.—T. C. B.

ADRENIN, Effects of, on the Distribution of the Blood. V. Volume Changes and Venous Discharge in the Intestines. Hoskins (R. G.) and Gunning (R. E. L.) Am. Jour. Physiol. (Balt.) 1917, xliii, 399.

Plethysmographic studies and determination of the outflow from the intestinal veins, under ether anesthesia, resulted most frequently in an augmentation of the gut volume, and of the discharge from the veins. The doses of adrenin injected varied from 0.25 to 8 cc of 1:100,000 solution. Often the dilatation phase was preceded by contraction, and in some instances contraction only occurred.

As the liver contracts under the influence of adrenin, it was necessary to determine to what extent the reactions of the intestines were due to back pressure from the liver. Several dogs were tested before and after the establishment of Eck fistulae. In all but one experiment there was no change in the reactions. In the one exception, shunting the portal blood directly into the vena cava converted an enterodilatation into an enterocontraction.—T. C. B.

(THYROID) The Effect of Thyroid on the Catalase Content of the Tissues. Burge (W. E.), Kennedy (J.) and Neill (A. J.) Am. Jour. Physiol. (Balt.) 1917, xliii, 433.

This investigation was undertaken to determine if thyroid feeding increases the catalase content of certain tissues, and thus accounts for increased oxidations in animals fed on thyroid, while in other tissues (muscles, fat) it causes a decrease which would account for the increased autolysis in these tissues.

After feeding cats on thyroid for at least five days, 25 cc of blood was collected and allowed to clot. The blood vessels were then washed free of blood with 0.9 per cent NaCl. The

various tissues were ground up in a hashing machine, and the catalase content determined by adding one gram to 45 cc hydrogen peroxide. The gas was collected over water in an inverted burette and reduced to standard atmospheric pressure. The blood was pressed through several thicknesses of cheese cloth and ground up in a mortar. Ten drops of this was added to 500 cc of hydrogen peroxide. In all cases the peroxide was diluted with an equal volume of distilled water.

The authors find that feeding thyroid increases the catalase of the blood and decreases it in the heart, and probably also in the fat and skeletal muscles. This will account for the increased oxidation in thyroid fed animals, and also for the increased autolysis of muscular tissues as indicated by loss of weight and strength.—T. C. B.

(THYROID) Effect of Thyroid Feeding upon Carbohydrate Metabolism. Kuriyama (S.) Am. Jour. Physiol. (Balt.) 1917, xliii, 481.

The glycogen content of the liver of white rats is distinctly decreased in three to five days of thyroid feeding. When thyroid feeding is discontinued the liver shows a normal glycogen content in two or three days. When dextrose is introduced parenterally in fasting rats the liver glycogen is increased in a few hours. This does not seem to be the case in thyroid-fed animals.

Experimental hyperthyroidism does not change the sugar content of the blood in either rats or rabbits.

Spontaneous glycosuria does not result from thyroid feeding in either rats or rabbits.

The tolerance of thyroid fed rabbits for dextrose, parenterally administered, does not differ from that of normal animals.

Nearly the same degree of hyperglycemia and glycosuria can be induced by adrenin injection in thyroid-fed as in control rabbits.

The adrenal gland of thyroid-fed rats contains approximately the same amount of adrenin as that of normal rats. —T. C. B.

PITUITARY, Experimental Operations on. Bell (W. B.) Quart. Jour. Exp. Physiol. (Lond.) 1917, xi, 78.

After a brief historical introduction there is a careful description of operative technique, fully illustrated. The experimental part deals with total and partial extirpation of the pituitary, clamping and separation of the stalk, and imitation tumors in the neighborhood of the pituitary.

Total extirpation of the pituitary is fatal, confirming the observations of Paulesco and of Cushing. Removal of very

large portions of the anterior lobe is also fatal. Removal of the pars posterior is without effect.

The most striking difference between Bell's results and those of Paulesco, Cushing and others is in the production of dystrophia adiposo-genitalis. In none of Bell's cases was partial removal of the pars anterior followed by this syndrome, although genital atrophy was usually found if there was a sufficient lapse of time after operation. Bell found, however, that dystrophia adiposo-genitalis occurred in two out of three cases where the stalk was clamped, or separated. In one case the increase in body weight amounted to 66 per cent in fifty-one days. Bell thinks the explanation of this fact lies in the view he has long held, that the pituitary is one organ, not two, and that the secretion can pass directly into the blood stream like other internal secretions, and not into the third ventricle, as held by Herring. Clamping of the stalk interferes with the blood supply to the organ, and causes atrophy of the cells of the pars anterior and intermedia.

Attention is called to the peculiar somnolent condition following operations which decrease the pituitary secretion. It was suggested by Gemelli that hibernation might be due to hypopituitarism, and the same shrunken, inactive cells are present in hibernation that are observed in experimental cases, and in dystrophia adiposo-genitalis in the human.

"Artificial tumors in the neighborhood of the sella turcica may produce irritation which is accompanied by glycosuria and emaciation; or by interfering with the blood supply may lead to degenerative changes in the cells of the pars anterior, and so give rise to the syndrome dystrophia adiposo-genitalis."—T. C. B.

Action of Gland Extracts and Drugs on the Uterus of the Rat. Itagaki (M.) Quart. Jour. Exp. Physiol. (Lond.) 1917, xi, 39.

For experimentation, the uterus of the rat offers certain advantages over that of larger animals. It is easily obtained. Being small, only a comparatively small quantity of the solution to be tested is required. The rhythmic spontaneous contractions in oxygenated Locke's solution at 37 deg. C is fairly regular. The results of the author's experiments may be briefly summarized: 1. Extract of posterior lobe of pituitary always produces an increase of tone. This corroborates the findings of Dale and others. 2. Solutions of adrenin inhibit rhythmic contractions, with or without diminution of tone. 3. Extract of thyroid occasionally produces increase of tone, but generally has no effect. 4. Extracts of orchitic substance, of uterus and of brain, have no appreciable effect.

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As for the drugs, the action of nicotine is variable, the action of pilocarpine is inconstant; weak solutions of atropine cause increase, stronger solutions diminution, of tone. Barium chloride stimulates.—T. C. B.

THYROID, Feeding of, on Weight of the Suprarenals and on their Adrenalin Content. Herring (P. T.) Quart. Jour. Exp. Physiol. (Lond.) 1917, xi, 47.

The feeding of 0.2-0.5 gm. of fresh ox thyroid to white rats results in an increase in the size and weight of the suprarenals, and also an increase of the adrenin content of these glands, confirming the observations of Hoskins on new-born animals. The hypertrophy involves both the cortex and medulla of the gland, and the author thinks there is "reason to believe that when accessory suprarenals are present, they, too, undergo enlargement." Reckoned in mg. per 100 gms. body weight, the increase may amount to as much as 76-78 per cent.

As the amount of adrenin in the blood is likely to vary, a "better index of any change in the adrenalin content of the body is furnished by an estimation of the amount in the suprarenal capsules and chromaphil tissues." Folin's micro-chemical method was used, and an increase of about 50 per cent over normal animals was observed. When present, accessory suprarenals probably also show an increase in adrenin.

The author notes that when rats are fed with thyroid they sometimes die suddenly, and post mortem shows cardiac hypertrophy. Investigations along this line are being continued.—T. C. B.

(THYROID) Carbohydrate Metabolism in Relation to the Thyroid Gland. II. The Effect of Thyroid Feeding on the Gaseous Metabolism. Cramer (W.) and McCall (R.) Quart. Jour. Exp. Physiol. (Lond.) 1917, xi, 59.

According to Cramer and Krause, feeding with thyroid causes complete disappearance of glycogen from the liver, yet there is no glycosuria as would be expected. There are three possible explanations of this apparent paradox: 1. The suspension of the glycogenic function of the liver is compensated for by an increased deposit of glycogen in the muscles. 2. The thyroid hormone has a direct stimulating effect on the oxidation of carbyhydrates. 3. The carbohydrates might be transformed into fats and deposited as such. The first possibility may be excluded, as there is no increase of muscle glycogen in thyroid-fed animals. The third possibility can be dismissed at once, since the fat rapidly disappears in animals fed on thyroid. As to the second possibility, that the thyroid directly stimulates the oxidation of carbohydrates, it may be excluded

on the ground that glycogen is "absent from the liver immediately after a meal rich in carbohydrates, whereas one would expect to find only a more rapid disappearance of glycogen from the liver of thyroid-fed animals and a replenishing after a meal, if the effects on the liver glycogen were merely a secondary one." Other facts confirm this conclusion. If the thyroid has a direct stimulating action on carbohydrates, one would expect to find a rise in the assimilation for sugar in Graves' disease, whereas there is a tendency to glycosuria in this condition. On the other hand, thyroid insufficiency ought to lower the sugar assimilation limit; but in myxedema there is the reverse tendency.

The authors think the condition in experimental hyperthyroidism cannot be explained by the orthodox conceptions of carbohydrate metabolism, and determined to approach the problem "without the bias of a theory." If, in experimental hyperthyroidism, the "carbohydrates are neither deposited, nor excreted as such, nor transformed into fats, we must arrive per exclusionem at the conclusion that they are oxidised." Their problem was to determine if this conclusion was justified. The observations were made on rats, and the gaseous metabolism was determined by the method of Haldane and Pembrey, with some modifications. The experiments were all carefully controlled.

From their observations Cramer and McCall conclude that the thyroid secretion produces an increased oxidation of carbohydrates. The action is not direct, but "follows its action in discharging glycogen from the liver." They distinguish an "early" stage (second or third day after feeding thyroid), and a "later" stage (third to sixth day). In the "early" stage the pre-existing carbohydrate of the food and of the deposits in the organism is oxidised. In the "later" stage there is, in addition, a formation of carbohydrates from protein and possibly also from fat, and a subsequent oxidation of carbohydrates thus formed." There is a marked rise in carbon dioxide excretion and oxygen absorption. Illustrative curves are reproduced.

"The action of the thyroid secretion on the glycogenic function of the liver lies thus at the root of the increased oxidation of proteins, carbohydrates and probably fats produced by thyroid feeding."—T. C. B.

CORPUS LUTEUM, Influence of Extracts upon Plain Muscle, Especially that of the Uterus. Itagaki (M.) Quart. Jour. Exp. Physiol. (Lond.) 1917, xi, 1.

In view of the conflicting evidence as to the action of extracts of corpus luteum on the contraction of the uterus, it

seemed "desirable to submit the subject to renewed investigation." The extracts in most cases were made from the corpus luteum of the cow, immediately upon receipt from the slaughter house; occasionally they were kept over night in an ice chest. The extracting medium was Locke's solution. The contractions were recorded by Schafer's modification of Magnus' method.

Using one of the cornua of the rat's uterus, the author finds that in the majority of cases "there is a marked increase of tone, having almost the appearance of tetanus." In rare cases the effect was just the opposite—diminution of tone, and even abolition of rhythmic movements. Strips of rabbit's uterus showed the same result, eight out of ten experiments giving stimulation, and two inhibition. Cats, dogs and guinea pigs, all gave increase of tone, with one exception in the case of cats, where there was inhibition. The effects were the same whether the uterus was pregnant or non-pregnant.

Itagaki thinks the difference in the action of extracts of corpus luteum on the uterus is due to the presence of two antagonistic substances. These substances can "sometimes" be separated by alcohol, the chalonic substance (inhibiting hormone) going into alcoholic solution. It is very small in amount, while the (stimulating) hormonic substance, soluble in water, but not in alcohol, ether or chloroform, is much larger in amount. The proof is not very convincing; extracts of the ash of corpus luteum cause inhibition in strong 5 per cent solution, due probably, as the author suggests, to the preponderance of potassium found in the ash of corpus luteum.

Corpus luteum extract generally produces relaxation of the intestine and bladder of the rat, but contraction of the whole intestinal tube of the rabbit and kitten; "although, when isolated strips of either the longitudinal or circular muscle of the intestine of these animals were taken they showed relaxation." No change in the frog's iris was observed. There was very little effect on blood pressure; if anything, there is a slight fall. There is no evidence that its action is through the nerve endings.—T. C. B.

(OVARIES) Action of Various Extracts obtained from the Cow's Ovaries upon the Muscular Tissue of the Uterus, Intestine and Blood Vessels. Itagaki (M.) Quart. Jour. Exp. Physiol. (Lond.) 1917, xi, 27.

In this paper the author describes the results of experiments with extracts of different parts of the ovary upon smooth muscle. Using an extract of part of the ovary about the hilum, he finds that out of forty experiments on the rat's

uterus "thirty-one showed diminution or inhibition of rhythmic movements, with or without relaxation of tone; five showed inhibition of rhythmic movements, followed after a time by a recurrence of contractions; in three no change was observed; in one there was increase of tone from the first."

"The uterus of other animals is affected differently, for in the rabbit, cat and guinea pig an extract of the hilum usually has the result of producing an increase of tone."

"Liquor folliculi produces an increase of tone of the uterine muscle in the rat, rabbit and cat, or at any rate an increase in height of the rhythmic contractions."

Extracts of the whole ovary produced diminution or complete inhibition of the rhythmic movements of the rat's uterus, but increase of tone or height of contractions in the rabbit, in four out of five cases.

"When applied to the whole thickness of the intestinal tube, all the extracts tested—hilum, liquor folliculi, whole ovary—determined an increase of tone, whereas a strip of the longitudinal coat of the rabbit's intestine is sent into relaxation by extracts of hilum."

Intravenous injection causes a fall of blood pressure in all cases.—T. C. B.

(CORPUS LUTEUM) The Cause of Hyperplasia and Secretion of the Mammary Gland. Athias (M.) C. R. Soc. de Biol. (Paris) 1916, lxxix, 557.

From the results published in a previous paper he concludes that the corpus luteum is not necessary for the development and secretion of the mammary gland. He suggests other structures that may be responsible for the development and secretion of the mammary gland.—F. A. H.

(SECRETIN) Action of Secretin on the Kidney. Piticarin (J.) C. R. Soc. de Biol (Paris) 1916, lxxix, 871.

See abstract, Endocrinology i, 71.—F. A. H.

(THYROID) Effects of Thyroid Removal upon the Development of the Gonads in the Larvae of Rana pipiens. Allen (B. M.) Science (Lancaster, Pa.) 1997, n. s. xlvi, 216.

The thyroid anlagen were removed at their inception. It has been shown in a previous article that the thyroidless tadpoles failed to undergo metamorphosis, although the size attained became much greater than in normal tadpoles. The gonads of these thyroidless tadpoles develop normally, as far as sexual maturity in the male and at least as far as the period when the ova are visible to the naked eye in the female.

F. A. H.

(ADRENIN) Absorption of Adrenin after Intratracheal Injection. Auer (J.) and Gates (Frederick L.) Jour Exp. Med. (Balt.) 1916, xxiii, 757.

Experiments were performed on rabbits under ether. Adrenin solution in 0.1 per cent strength was injected into the respiratory passages, into the tracheal cannula, into a bronchus by means of a catheter, or directly into the lung tissue by passing a hypodermic needle through the chest wall. The dose varied from 0.15 to 0.03 cc. per kilo of body weight.

The absorption of adrenin caused a marked rise of blood pressure in a few seconds, which lasted from six to ten minutes. As a result of their experiments with adrenin the authors conclude that the intratracheal path would be useful in the administration of other substances.—F. A. H.

(CORPUS LUTEUM) Histological Study of Ovaries Grafted upon Castrated Pigs and Removed After the Establishment of Lacteal Secretions. Athias (M.) C. R. Soc. de Biol. (Paris) 1916, lxxix, 553.

Ovaries from both virgin and non-virgin guinea pigs were employed in making the grafts.

The author studied eight grafts, of which four were taken during the first three days of secretion of the mammary gland. False corpora lutea are found in these grafts, but in no instance did he find a true corpus luteum.—F. A. H.

(TESTIS) On the Occurrence of Spermine. Rosenheim (M. C.) Jour. Physiol. (Lond.) 1917, li, 4.

The author has isolated spermine from testis, pancreas, spleen, brain, cancerous lymphatic tissues, cod's roe, Liebig's meat extract. She was unable to isolate the substance from serum, blood or protein-free milk. Yeast was the most convenient source of preparation. Evidence supports the view that spermine is an aliphatic base.—F. A. H.

(PITUITARY) Pituitary Standardization. Hamilton (H. C.) and Rowe (L. W.) Jour. Lab. Clin. Med (St. Louis) 1916, ii, 120.

The authors found the pressor test more dependable than the uterus test, because of the great variation in sensitiveness of different specimens of uterus. They believe that the pressor test is an indicator of the oxytocic value.

By injecting small amounts of pituitary extract and allowing not less than fifteen-minute intervals, often between twenty and thirty doses of 0.05 cc Pituitrin (Parke-Davis) have been injected intravenously into dogs without the depressant effect becoming increased.—F. A. H.

(ADRENIN) On the Pharmacology of the Ureter. I. Action of Epinephrin, Ergotoxin and of Nicotin. Macht (D. I.) Jour. Pharm. and Exper. Ther. (Balt.) 1916, viii, 155.

Longitudinal strips and rings of the ureters of pigs and oxen were employed. Adrenin increased the rate of ureteral contractions and the tonus of the ureter, large doses producing a tonic spasm. After previous administration of ergotoxin adrenin inhibits the ureteral contractions. Adrenin produced similar effects upon the human ureter.—F. A. H.

(ADRENIN) Effect of Epinephrin on the Medullary Centers. Brown (E. D.) Jour. Pharm. and Exper. Ther. (Balt.) 1916, viii, 195.

The medulla of dogs was perfused by a mixture of defibrinated blood and either Ringer-Langendorff solution or a 0.9 per cent solution of sodium chloride entering the carotid and vertebral arteries.

In a majority of cases where adrenin was introduced into the perfusion mixture there was slowing of the heart and a fall in blood pressure. Adrenin seemed to act directly upon the vagus center because the slowing of the heart was immediate and was not connected with a rise in blood pressure. Occasionally there was a lowering of the blood pressure without slowing of the heart.

Small doses of adrenin often increased both the depth and rate of the respiration, while large doses usually diminished the depth and rate or might even stop respiration.—F. A. H.

(THYROID) Therapeutic Applications of Human Thyroid Extract. Beebe (S. P.) N. Y. Med. Jour. (N. Y.) 1916, civ, 445.

Certain cases of hypothyroidism, in which the administration of animal thyroid preparations only partially controlled the symptoms, were almost completely relieved by human thyroid extracts.

A method for the preparation of human thyroid extracts is described.—F. A. H.

(PANCREAS) Influence of Pancreatic Extracts on the Production of Lactic Acid in Surviving Muscles. Winfield (G.) and Hopkins (F. G.) Jour. Physiol. (Lond.) 1915, 1, 5.

Pancreatic extract has an inhibitory action on the formation of lactic acid in surviving muscle. The responsible factor is heat stable.—F. A. H.

(PITUITARY) Studies on the Properties and Action of Tethelin. Schmidt (C. L. A.) Jour. Lab. and Clin. Med. 1917, ii, 711.

The properties and action of tethelin, the active principle of the anterior lobe of the pituitary body, have been studied. It was found that tethelin is nonantigenic and nontoxic; hence its use therapeutically is warranted. It cannot be used as the antigen in the Wassermann test, has no effect on the proteins of blood serum, does not cause a specific hyperleucocytosis, can be used as a medium for the growth of certain bacteria, is not split by trypsin or lipase, and does not stimulate contraction of the isolated cat or guinea pig uterus.—Author's Summary.

(PITUITARY) On the Possible Derivation of the Active Principle of the Posterior Lobe of the Pituitary Body from the Tethelin Produced by the Anterior Lobe. Schmidt (C. L. A.) and May (E. S.) Jour. Lab. and Clin. Med. (St. Louis) 1917, ii, 708.

The authors investigated the possibility of the production of the pharmacodynamic substance found in posterior lobe extracts from an inactive secretion of the anterior lobe. They found that treatment of tethelin with barium hydroxid gave rise to a substance having both the uterus-stimulating and the blood pressure raising property of posterior lobe extracts.

R. G. H.

(PITUITARY) Physiology of the Pituitary Gland, and the Actions of its Extracts. Cadwaller (J. C.) Lancet-Clinic (Cinc.) 1916, cxv, 33.

A brief review.—F. A. H.

(SEX) The Accessory Chromosome in the Frog Possessing Marked Hermaphroditic Tendencies. Swindle (W. W.) Biol. Bull. (Woods Hole) xxxiii, 70.

The number of chromosomes in the germ cells of the frog (Rana pipiens) is twenty-five in the male and twenty-six in the female. In the latter there appears at one stage a chromatin body that seems to be an accessory (sex-determining) chromosome. In an hermaphroditic frog there was an unequal distribution of chromatin to the daughter cells during the first maturation division. This may account for the presence of these individuals with hermaphroditic tendencies in this species of frog.—E. R. H.

(OVARY) The Experimental Production of Hypotypical Ovaries through Underfeeding. A Contribution to the Analysis of Sterility. Loeb (L.) Biol. Bull. (Woods Hole) xxxiii, 91.

In female guinea pigs which were underfed "hypotypical" (not properly developed) follicles were found in 69 per

cent of the cases examined (twenty-six animals) and the uterus was in the resting condition and smaller than normal. None of the follicles matured. In these typical follicles the granulosa cells degenerate early from lack of proper nourishment. The larger follicles are more readily affected than the smaller (younger) follicles.)—E. R. H.

(THYMUS) Experiments with Feeding Thymus Glands to Frog Larvae. Swindle (W. W.) Biol. Bull. (Woods Hole) xxxiii, 116.

The author fed fresh thymus and commercial powdered thymus to the larvae of R. pipiens and other species. One hundred and twenty-five larvae were fed fresh thymus and an equal number were fed liver. The thymus had no effect upon the growth nor upon metamorphosis of the animals as compared with liver-fed larvae. In other series, fed powdered thymus, there was no effect upon growth, but there was a slight retardation of metamorphosis, which, however, the author regards as too small to be important on account of the extent of normal variability. The gonads were not affected. The author concludes logically that thymus has no effect when fed to frog larvae. This is in keeping with the growing belief that the thymus is not concerned with general metabolism. It is possibly merely a hematopoietic organ such as it appears to be when examined microscopically, and not an endocrine structure at all.—E. R. H.

(PANCREAS) Studies in Experimental Diabetes after Pancreatecomy. Epstein (A. A.) and Baehr (G.) Jour. Biol. Chem. (Balt.) 1916, xxiv, 1.

The authors were able to produce excessive hyperglycemia in cats by totally extirpating the pancreas. The amount of blood sugar was estimated by a micro method of their own by which they were able to work with as small samples as 0.1 cc. to 0.2 cc. They noted that after pancreatectomy animals were very thirsty and drank large volumes of water. Investigation showed that this increased ingestion of fluid increased the blood volume as much as 50 per cent. Their percentages of blood sugar are corrected on the basis of the original volume. The volume increase of blood was determined by finding proportion between blood plasma and cells.

After removal of the pancreas blood sugar rose from .084 per cent to .431 per cent in twenty-six hours. It stayed constant until about the one hundredth hour, when it jumped to .603 per cent, from which time the increase was progressive; at 141 hours it was .838 per cent, and the emaciated animal became stuporous. This terminal rise occurred in three other cats. Simultaneous with progressive hyperglycemia was a

diminished glycosuria. After the eighty-fourth hour there was no sugar, and after the 108th no acetone in the urine. Albuminuria was progressive. It was thought that these conditions might have been the result of renal insufficiency, so that in six other cats—three nourished and three starved nine days—the pancreas and both kidneys were removed. Animals drank water copiously as before. In well-nourished cat blood volume increased as much as 58 per cent, while blood sugar rose from .085 per cent to 1.713 per cent, or more than twenty fold, while liver and muscle contained .42 per cent and .99 per cent glycogen respectively, as against .14.4 per cent and 1.7 per cent in control cat not operated upon. With the starved cats the blood volume increased as much as 65 per cent after forty-eight hours and blood sugar from .58 per cent to 1.980 per cent, or thirty-four times, while glycogen in liver and muscle was 0.0 and 0.06 respectively. Hyperglycemia developed earlier in nourished than starved cats.

The author believes that the hyperglycemia in experimental diabetes in cats mounts progressively in the terminal stages because of diminished permeability of the kidneys. This would furnish an explanation of the excessive rise in the blood sugar of diabetics prior to the development of coma. Experimental interference with glycosuria of depancreatized animals brings about a rapidly progressing hyperglycemia caused by a mobilization of carbohydrate from the liver and muscles. Detailed tables of experimental work accompany the original article.—J. R. M.

(PARATHYROID) Some Observations on the Tetany of Parathyroidectomized Dogs. Greenwald (I.) Jour. Biol. Chem. (Balt.) 1916, xxv, 223.

Greenwald has endeavored to determine the cause of the parathyroid tetany in dogs. In a previous paper he reported that there was a marked retention of phosphorus after parathyroidectomy, and that this retention was followed or accompanied, but never preceded by, a retention of sodium and potassium. Experimental work shows the impossibility of phosphorus retention as O-phosphate acting as the cause of tetany. Attempts were made to show a probability of inosinic acid as the cause of tetany. This is one of the simplest nucleic acids; upon hydrolysis it yields, beside phosphoric acid, a pentose, d-ribose and hypoxanthine. The latter produces convulsions in frogs. Intravenous injections of xanthine causes tetany in dogs similar to parathyroid tetany.

A solution of sodium inosinate prepared from the barium salt was injected intravenously into a dog from which the thyroids and parathyroids had been removed five hours previ-

ously. Results were negative. Determinations made after injection and after tetany appeared showed that amount of acid-soluble phosphorus in serum was less than in the first instance. The hypothesis that inosinic acid is the toxic agent in the tetany of parathyroidectomized dogs must be abandoned.—J. R. M.

(ADRENAL) The Effect of Certain Procedures upon the Course of Fatigue in Frog's Muscle. Crider (J. O.) and Robinson (W. W.) Am. Jour. Physiol. (Balt.) 1916, xli, 376.

This article is not primarily of endocrine interest. The author finds that the ligation of one leg of the frog and the excision of the gastrocnemius of that leg increases the working power of the other leg when the latter is excised after a wait of thirty minutes between the two excisions. He suggests that the ligation of one leg may bring about an increase in the working power of the other leg by reflexly causing an increase in blood pressure and thus improving the circulation of the non-ligated leg during the thirty minutes' wait. He suggests that this may also be due in part to secretion of adrenin following the operative proceedings. He gives five pages of tables showing his experimental work.—J. R. M.

(ADRENAL) Le role des surrénales dans l'hypertension artérielle consécutive aux embolies cérébrales. (The Part played by the Adrenals in Arterial Hypertension following Cerebral Embolism.) Roger (H.) C. R. Soc. de Biol. (Paris) 1917, lxxx, 427.

Cerebral embolism was produced in the rabbit by injection of lycopodium into the carotid artery. This is followed by an initial fall in blood pressure, then a marked rise in blood pressure which persists. If the adrenals have been removed the blood pressure soon returns to normal. The author concludes that the first rise in blood pressure is due to nervous excitation resulting from the embolism, while the permanent hypertension is due to the secondary action of the adrenals. —F. A. H.

(ADRENIN) Lé sécrétion surrénale d'adrénaline ne tient pas sous sa dépendance l'effet vaso-constricteur du sang asphyxique. (The Vasoconstrictor Effect of Asphyxiated Blood Does Not Depend upon the Secretion of Adrenalin from the Adrenals.) Gley (E.) and Quinquaud (Alf.) C. R. Soc. de Biol. (Paris) 1917, lxxx, 15.

The authors found that suppression of the adrenal secretion did not diminish the vasoconstrictor effect due to asphyxia.—F. A. H.

(THYROID) The Influence of Partial Thyroidectomy in Pigs. Palmer (C. C.) Am. Jour. Physiol. (Balt.) 1917, xliii, 572.

Palmer reports the results of thyroidectomy on six young pigs from the same litter with the view of establishing the probability of inducing cretinism. The main thyroid was excised from three and three were controls.

He gives a very complete exposition of the anatomy of the thyroid in the pig, pointing out the position, size, etc., of the thyroids and parathyroids at varying ages, both before and after birth. After excising the main thyroid at the ages eight, twelve and fifteen days respectively no differences were noted between operated and control pigs until they were two months old. Then a much lowered resistance was apparent in those operated upon. This was made evident by susceptibility to parasitism, by slowness of injuries to heal and by skin lesions on the abdomens of two. These troubles continued till the autumn, when the pigs were about six months old, at which time, with the advent of cold weather, all became very much improved; the improvement was especially notable in the case of the operated pigs. These did not gain in weight as rapidly as the controls, but became more healthy looking. Body temperature taken at frequent intervals showed no variation from normal. At forty weeks (maturity) the average weight of the operated pigs was thirty pounds under controls. Sexually all males were active. Two sows (operated and check) were bred to an operated boar; both conceived; post mortem shortly before parturition time showed in the normal sow one fully formed fetus and in the operated sow one mummified fetus. When about ten months old three thyroidectomized and one check developed pneumonia and pleurisy and all died inside of two weeks. Post mortems showed extensive tissue changes in operated pigs which died from pneumonia, but only slight lung lesions in the check.

The author believes that extirpation of the main thyroid does not induce cretinism within a year. Growth is retarded and resistance is lowered, but otherwise the operated pigs are apparently normal. A post mortem examination shows marked hypertrophy of accessory thyroid tissue, but the accessory thyroid cannot completely compensate. In pigs the degree of hypothyroidism which occurs is insufficient markedly to change the physical appearance, but it lowers resistance to infection and impairs the function of reproduction.—J. R. M.

(THYROID) Recherches expérimentales sur l' "hyperthyreosis" et l' "athyreosis" et sur quelques actions de l'adrénaline. (Experimental Researches on Hyperthyreosis and Athyreosis and Some Effects of Adrenalin.) Albertoni (P.) Arch. Ital. de Biol. (Pisa) 1916, lxv, 63.

The excitability of the cardiac vagus in the dog and rabbit was diminished after prolonged administration of large doses of thyroid, such as are necessary to produce hyperthyroidism.

The author describes the symptoms produced by prolonged thyroid feeding.

There was a large increase in the amount of water in the blood, liver and kidney, while that in the muscles decreased. The liver contained very little glycogen, but showed an increase in nitrogen. The brain had not changed in water or nitrogen content.

After extirpation of the thyroid in a dog, substances with hypotensive action accumulated in the blood.

The experiments of Sutherland Simpson on sheep were confirmed. No ill effects resulted from removal of the parathyroid and thyroid in the adult sheep or goat.

Albertoni produced hemorrhage in the brain of a dog by the injection of two doses of adrenalin 1:1000, one cubic centimeter in each dose. As a result, paraplegia developed.

F. A. H.

(PITUITARY) Concerning the Action of Various Pituitary Extracts upon the Isolated Intestinal Loop. Shamoff (V. N.) Am. Jour. Physiol. .(Balt.) 1916, xxxix, 268.

From experiments described it is concluded "that certain posterior lobe preparations are capable of producing relaxation of the isolated intestinal loop and of inhibiting its rhythmic contractions, resembling in this respect the extracts of the adrenal medulla."

"In view of the foregoing observations, it may be stated that there exists in the posterior lobe of the pituitary body some substance which has an action on the isolated intestinal loop resembling the action of adrenalin, a substance moreover which may be other than that which raises blood pressure and causes diuresis. The substance is not constant in the extractives prepared in the usual ways, and may indeed be inconstant in the fresh glands from which these substances are prepared." —T. C. B.

(PITUITARY) On the Secretory Discharge of the Pituitary Body Produced by Stimulation of the Superior Cervical Sympathetic Ganglion. Shamoff (V. N.) Am. Jour. Physiol. (Balt.) 1916, xxxix, 279.

A continuation of the work of Weed, Cushing and Jacobson, and deals with the effect on the urinary secretion, of stimulation of the cervical sympathetic ganglion.

As a rule, stimulation of the superior cervical ganglion results in a decided diuresis, resembling that which follows an intravenous injection of posterior lobe extract. The increased

flow of urine is independent of the elevation of blood pressure, for it often takes place at the moment of the lowest depressor phase. Glycosuria was also observed. All nervous influences to the kidney were excluded by section of the vago-sympathetics and section of the spinal cord at the fourth thoracic segment. The conclusion is that stimulation of the ganglion causes a secretion from the pituitary.—T. C. B.

(ADRENIN) The Relation of the Rate of the Spontaneous Liberation of Epinephrin to the Rate of Blood Flow through the Adrenals. Stewart (G. N.) and Rogoff (J. M.) Am. Jour. Physiol. (Balt.) 1917, xliv, 149.

In previous papers the authors have shown that in the cat the output from the adrenals is fairly constant over a wide range in the rate of blood flow, the concentration in the adrenal vein blood varying inversely as the flow. The present paper deals especially with the question whether with such quantitive methods as have been employed (rabbit's intestine and uterine segments) an exact inverse ratio between epinephrin concentration and adrenal blood flow can be made out.

The paper is largely taken up with protocols and their discussion, and the conclusion is reached that within the limits of error of the method used the concentration of epinephrin in blood from a "cava pocket" varies inversely as the blood flow through the glands, the rate of output of epinephrin being constant. The rule fails when the rate of blood flow falls below the value at which the concentration of epinephrin has reached the possible maximum.—T. C. B.

ADRENIN, Effects on Distribution of the Blood. VI. Venous Discharge from the Thyroid Glands. Gunning (R. E. L.) Am. Jour. Physiol. (Balt.) 1917, xliv, 215.

Adrenin in all doses causes vasoconstriction in the thyroid. There is a slight tendency to over recovery, due probably to vascular fatigue.

The apparent paradox that increased secretory activity is accompanied by vasoconstriction is explained by supposing that the gland stores its active substance, and discharges it periodically in response to emergencies. If this be the case, no anabolic activities are necessary at the time of discharge and hence there is no need for immediate functional hyperemia.—T. C. B.

ADRENIN, Action of, on the Blood. Menten (M. L.) Am. Jour. Physiol. (Balt.) 1917, xliv, 176.

Spectroscopic examination of the blood from the adrenal vein shows the absorption bands of oxyhemoglobin nearly as well marked as in blood from the carotid artery, indicating that adrenin causes increased formation of oxyhemoglobin. The

same is true when adrenin is added to venous blood drawn from other parts of the body. Attention is called to the fact that the increase in oxyhemoglobin is greater in blood drawn without anesthesia than in blood drawn under the influence of ether or chloroform, and that this should be taken as a factor in interpreting experiments on the action of adrenin in vivo.

The bright color of oxyhemoglobin is gradually replaced by a darker color of some other hemoglobin compound when adrenal blood is kept a few hours with a minimum of oxygen. This substance gives the spectrum of urobilin. Microscopically the erythrocytes are seen to be disintegrated. Here, too, ether has a retarding influence.

It has been shown that increase of OH ions is a factor in augmenting the formation of oxyhemoglobin, and Menten and Crile have reported that adding adrenin to serum or venous blood increases the OH concentration. Menten points out that this may explain in part at least the tonic influence of adrenin on the heart. Haldane's observation that the oxygen tension in the lung capillaries is greater than in the alveoli may also be explained by the fact that the affinity for oxygen is increased by adrenin. The observations of Cannon that in asphyxia and emotional disturbances where there is urgent need for oxygen there is an increase in the secretion of adrenin, also supports this view.—T. C. B.

(GONADS) On the Internal Secretion of the Sexual Glands. Lipschütz (Alex.) Jour. Physiol. (Lond.), 1917, li, 283

Steinach has shown that the internal secretions from the gonads act in a sex-specific manner. The male gonads cause development of the male sex characters only, inhibiting the development of the female characters, and vice versa. The author had the opportunity of examining some of Steinach's animals, operated on a few years ago.

In addition to the signs of a "successful masculation" of a female guinea-pig, there is a growth of skin at the urethric tubercle resembling a male preputium, and when this is drawn back there are two excrescences that are evidently the corp. cav. clitoridis which have changed into corp. cav. penis. The developed organ gives the impression of a hypospadic penis. Two spikes have developed, similar to the "horny spikes" in the normal male.

The average temperature of normal female guinea-pigs is higher than that of the male by nearly a degree. It is found that "feminized males" have a temperature approaching that of normal females.

Judging by the references this paper is based on reports published in the Anz.d.Akad.d.Wiss. in Wien, 1916 and 1917. —T. C. B.

(ADRENIN) The Mechanism for Vasodilatation from Adrenalin. Hartman (F. A.) and Fraser (L. McP.) Am. Jour. Physiol. (Balt.) 1917, xliv, 353.

In attempting to explain the action of adrenalin in dilating the intestine, the authors found that if the splanchnics were cut constriction replaced dilatation; this led to the study of the part played by the central nervous system in adrenalin vasodilatation.

Volume changes in the small intestine were studied after all connection with the nervous system were severed, the dilating dose of adrenalin having been previously determined. Three dogs and four cats were studied, and in every case but one dilatation was replaced by constriction when the splanchnics were cut, and the coeliac and superior mesenteric ganglia were removed.

Simultaneous plethysmographic records were made of the two hind limbs, one of which was denervated by cutting the femoral and sciatic nerves as high as possible. Small doses of adrenalin usually gave dilatation of the normal limb and constriction of the denervated limb. Large doses, such as those which usually produce a rise in blood pressure, caused constriction in both limbs.

Perfusion experiments were also tried. The circulation was cut off in the part to be studied (limb or intestinal loop), and oxygenated Ringer was perfused. Under these conditions injection of adrenalin into the general circulation resulted in dilatation of the intestine, and an increase in the volume of the hind limb, indicating vasodilatation.

The failures that occurred were in animals that were not normal. Disease, emaciation, intoxication with alcohol and anocain, asphyxia may cause inhibition of the vasodilator mechanism. It also seems that afferent impulses due to cooling or cutting the muscles of a limb, may impair or inhibit the adrenalin dilator reaction.—T. C. B.

CLINICAL STUDY

(THYROID) Early Diagnosis of a Case of Myxedeme Fruste. Wechsler (I. S.) J. A. M. A. (Chgo.) 1916, lxvi, 1549.

Wechsler mentions briefly the incomplete form of myxedema described by Hertoghe and reports a case in a woman of twenty-one, who complained nine months after parturition of diffuse headaches, sense of tiredness, profuse menstruation, sparse hair in outer one-third of eyebrows, dry skin and falling hair. She was instructed to wean the child and to take one grain of thyroid extract t. i. d. Treatment was continued for two months, and four months later none of the symptoms mentioned were in evidence.—F. C. P.

(PANCREAS) Endocrinopathic Inheritance. Stein (I. F.) J. A. M. A. (Chgo.) 1916, lxvi, 1811.

A brief report, with heredity chart, of a diabetic family, in which one member of the first generation suffered with diabetes; in the second generation there were seven members of the family, and three had diabetes; one woman (normal) in this second generation married a man with a simple goiter; in the third generation all members (eleven) are reported as normal; one member of the fourth generation (twelve members) was moderately obese. Stein states that this family does not bear out the conclusions of Timme (J. A. M. A. 1916, lxvi, 1438) that the inheritance of endocrine defects follows Mendelian laws.—F. C. P.

(PITUITARY) A Case Bearing on the Function of the Pituitary Body. Boyd (W.) J. A. M. A. (Chgo.) 1917, lxviii, 111.

After briefly reviewing the anatomy and physiology of the pituitary gland and quoting points from Cushing and Goetsch bearing on his case, Boyd reports a case of glioma of the floor of the third ventricle involving the left optic nerve and the infundibular stalk.

A boy of ten and one-half years complained of headache and vomiting and an inability to see more than one-half of the clock. Eye examination revealed nothing. Seven months later the examination of the eyes showed right eye 20-70 vision; left eye only feeble light perception; exophthalmos; dilated, sluggishly reacting pupils; no visual field on the left side; right temporal hemianopsia with reversal of the color fields and hazy injected disks with dilated and tortuous retinal vessels. A roentgenogram showed slight enlargement of the sella, with thinning of the bony walls. Sugar tolerance was greatly increased. There was no thermal response to injections of anterior lobe of the hypophysis. Operation via the transsphenoidal

route revealed a soft translucent struma extruding from the floor of the sella. As much of the tumor was removed as seemed advisable. On November 21 the patient became semicomatose and developed convulsions. Death occurred on the third day. At autopsy, the pituitary body appeared normal. In the interpeduncular space apparently growing from the floor of the third ventricle, surrounding the left second nerve and the infundibular stalk, there was a soft, grayish mass. Microscopically, the tumor proved to be a glioma.

The author believes this case to be additional proof that the secretions of the posterior lobe of the pituitary pass to the third ventricle via the infundibulum.—F. C. P.

(CAROTID BODY) A Case of Tumor of the Carotid Body. Cahill (G. F.) and Taylor (R. M.) J. A. M. A. (Chgo.(lxviii, 1898.

A Russian Jewess, age fifty-one, with a tumor on the right side of the neck. Tumor mass present eight years, but small until one year ago, when it began to grow slowly. It caused no symptoms. Tumor felt lobulated and was not movable. At operation a lobulated, reddish, roughly rounded mass, 4 cm. in diameter, was found very firmly attached to the deep structures of the neck. It was located between the external and internal carotids, extended down into the bifurcation and surrounded the internal jugular vein. The microscopical examination showed the characteristic picture of the carotid body. —F. C. P.

(THYROID) Tonsillar Endamebiasis and Thyroid Disturbances. Evans (J. S.), Middleton (W. S.) and Smith (A. J.) Am. Jour. Med. Sci. (Phila.) 1916, cli, 210.

Tonsillar lesions of an infective cryptic character were found in 22.8 per cent, and nasal together with tonsillar lesions existed in 90 per cent of 362 goiterous individuals examined from this standpoint. In typically diseased tonsils, out of thirty-four cases examined microscopically 97 per cent were found to harbor endameba gingivalis (Gros) in the tonsillar crypts. Of sixteen individuals of this group who after treatment by means of emetin hydrochloride were re-examined, thirteen, or 81 per cent, were shown no longer to have endamebae in the cryptal contents. In twenty-three individuals to whom emetin was administered a reduction in the bulk of the goiter was appreciable in eighteen individuals, and in seven dysthyroid cases included in this group of treated cases six were benefited in degrees varying from slight amelioration to apparent cure. Inability to demonstrate endamebae in the thyroid gland renders improbable any direct causal relation of the amebic infestment of the tonsils per se to the develop-

ment of thyroid disturbances. However, the improvement, morphologically and symptomatically, in the treated cases leaves little doubt, after ruling out a vasomotor influence from the emetin employed, as to an indirect relationship. A symbiosis of endamebae with appropriate bacteria, leading to the elaboration and absorption into the thyroid of selective thyrotoxic poisons, is at least conceivable in explanation of such relation. In no sense do the writers care to be understood as advancing other locations of infections capable of producing thyrotoxic toxins, perhaps, too, toxic substances having similar influence but derived from metabolic or alimentary fault, or even entering the body from without, are all of possible influence; nor is the influence of sympathetic stimulation, however accomplished, to be overlooked.

The writers are unable to reach any satisfactory explanation of the known occurrence of belts of endemic goiter along certain well defined glacier drifts.

(It should be noted that Nowlin (Jour. Parasit. July, 1917) was unable to find amebae in the tonsils in one or more cases of seven pyorrhea with amebiasis.)—G. H. H.

(THYROID) Studies of the Basal Metabolism in Disease and their Importance in Clinical Medicine. Means (J. H.) Bost. Med. and Surg. Jour., 1916, clxxiv, 863.

The author concludes that basal metabolism can be readily studied in a hospital clinic with comparatively inexpensive apparatus. The normal basal metabolism is fairly constant, and hence wide variations from it in disease are of interest to the clinician. A marked rise occurs in hyperthyroidism and a marked fall in hypothyroidism. In regard to hyperthyroidism it seems probable that the basal metabolism furnishes: (a) The best index as to the severity of the disease, and hence is a quantitative means of following the course and of judging of the effectiveness of treatment, and (b) a valuable aid in differential diagnosis. Enormous grades of obesity are possible in the presence of a normal basal metabolism. When a reduction in the metabolism was found in obese subjects there was also clinical evidence of a defective internal secretion. A clearer conception of the food requirements in disease is furnished by the basal metabolism than by any other factor.—G. H. H.

(PITUITARY) Acromegaly with Extreme Degree of Exophthalmos. Weidler (W. B.) Bost. Med. and Surg. Jour., 1916, clxxiv, 506.

Weidler presents the symptoms and findings in a progressive case wherein the X-ray shows enlargement of the base of the sella and of the posterior clinoid processes. He summarizes his findings thus:

1. Gradual onset and progress of the cephalic changes, but more especially of the brows, ears, nose and lower jaw, the protruding abdomen, sloping shoulders, trouble with the feet and hands.

2. Gradual decrease of sexual desire and sexual power, and loss of physical strength.

3. Exophthalmos and changes noted in the field of vision make one think that this is a case of acromegaly without any of the well-marked symptoms, which will undoubtedly be present in a later stage of this patient's disease.—G. H. H.

(OVARY) Progress in the Study of Ovarian Transplantation and Ovarian Secretion. Martin (F. H.) Surg. Gyn. & Obs. (Chgo.) 1917, xxv, 336.

The review of the literature for the past two years serves to confirm the conclusions arrived at two years ago, namely, that so far the only form of ovarian transplantation that is practicable is autotransplantation, and that this has a rather limited field of usefulness in the retardation and modification of the symptoms of the artificial menopause brought about by complete removal of the ovaries. In spite of the perhaps overenthusiastic conclusions of a few workers, neither homo- nor heterotransplantation has as yet justified its use in human surgery. The great problem yet remaining to be solved in ovarian transplantation is to find some means of overcoming the resistance of the body to homografts, for this is the only means of opening up a wide field of usefulness for the operation. The way to a solution of the problem lies through a closer study of the internal secretion, not only of the ovary itself, but of the other glands of internal secretion, all of which seem to be so closely interrelated that absolute separation of their functions seems impossible. Some hopeful work has been done in endeavoring to find substances which will inhibit the resistance of the host to the graft, but for the most part the work still remains to be done, and the surgeon in adopting ovarian grafting, instead of solving a problem, has rather opened up a greater one which awaits solution by the serologist and endocrinologist.—Author's Summary.

OVARY, Its Relation to the Uterus and Mammary Gland from the Experimental Aspect. Loeb (L.) Surg. Gyn. & Obs. (Chgo.) 1917, xxv, 300.

The ovary is a complex gland of which the most important constituents are follicles in various stages of growth and atresia, and corpora lutea. In addition, we find in some species interstitial gland and sometimes embryonic structures developing parthenogenetically from eggs. Cyclical changes occur both in the ovary and secondarily in the uterus and mammary

gland. The primary cyclical changes in the ovary are in sequence: follicle ripening, ovulation, corpus luteum formation. In some species ovulation is accompanied by degeneration of all but the smallest follicles.

An elaborate self-regulating mechanism controls ovulation. Normally the corpus luteum inhibits ovulation. During pregnancy the life of the corpus luteum is prolonged. Experimentally ovulation can be influenced at will, accelerated by excising all corpora lutea, or retarded by producing artificial deciduomata. The retarding action of the corpus luteum is chemical, not mechanical.

The corpus luteum has a sensitizing action upon the uterus. This action can be analyzed by experimental methods. If the uterus is incised or mechanically stimulated at the time during which the corpus luteum is elaborating this growth substance, maternal placenta (deciduoma) is formed. The mechanical stimuli, therefore, assume in this respect the function which the ovum exerts under normal conditions. The form of growth response of each species is characteristic. The localization of sensitization varies in different species, being limited to the uterus in rabbits and guinea pigs, but distributed more widely in the human female. No specificity exists in the sensitizing substance given off by the corpus luteum as far as different individuals of the same species are concerned. The life period of experimental deciduomata is short except in pregnancy, during which their persistence is prolonged. Corresponding to and dependent upon the cyclical ovarian changes, uterine cyclical changes occur. The cycle consists of heat, regression and interval. Heat probably is due to maturation of the follicles and dependent upon the absence of the corpora lutea; growth activity is the result of corpus luteum secretion; regression marks the cessation of corpus luteum secretion, which is followed in the interval by a condition of rest. Pregnancy causing a persistence of the corpus luteum is characterized by an accentuation but not a prolongation of the active phase, and an inhibition of the uterine cyclical changes throughout gestation.

While it is possible to produce experimentally during pregnancy a new ovarian cycle, through incision of the corpora lutea, such a new ovarian cycle is not followed by a new uterine cycle. During pregnancy a mechanism is at work preventing the uterine mucosa from responding to the stimuli given off by various ovarian structures. It follows that the corpus luteum subserves at least two functions, inhibiting ovulation and producing a substance which causes growth in the uterus.

The ovary shows other non-cyclical functions. It has a trophic influence on the genitals and either primarily or sec-

ondarily determines the development of the secondary sexual characters. The ovary likewise controls the development of the mammary gland. It exerts a trophic influence on this organ and determines its normal cycle. During heat and subsequent to ovulation proliferative changes occur; these cease while the corpus luteum develops and functionates. The incidence of breast cancer in mice is greatly reduced by castration.—Author's Summary.

ADRENALS, The Experimental and Clinical Evidence as to their Influence Exerted upon the Genital System. Vincent (S.) Surg. Gyn. & Obs. (Chgo.) 1917, xxv, 294.

What we call the adrenal body represents the anatomical association of two elements, each of which is derived from a separate and independent system. The adrenal proper, or "cortex," is part of the "cortical" or "interrenal" system. The medulla is simply an accumulation of chromaphil cells of the same nature histologically, chemically and pharmacodynamically, as similar masses of cells in other parts of the body. There is no clear evidence that these two systems are functionally related. The adrenal medulla (as well as the chromaphil tissue generally) is developed from the sympathetic nervous system. Its duty seems to be to facilitate the functions of this system in certain physiological emergencies. The adrenal cortex (as well as the "accessory cortical adrenals") is developed from the germ epithelium, and the evidence is now strongly in favor of the view that it has certain important functions in connection with the development and growth of the sex organs. There is a considerable amount of clinical evidence that tumors of the adrenal cortex are frequently associated with sex abnormalities. The clinical evidence also favors the view that when cortical tumors occur in the female an accentuation of male secondary sexual characteristics develops, and simultaneously a hypoplastic condition of the internal generative organs supervenes. Additional evidences as to a connection between adrenal cortex and the sexual organs is furnished by the enlargement of the cortex during breeding and pregnancy. Feeding young animals with adrenal gland substance seems to stimulate the growth of the testes. It is possible that a final solution of the problem will only be arrived at when the more general problem of the relationship between the ductless glands shall have been solved.—Author's Summary.

PANCREAS, Its Endocrine Function and Its Relation to the Sex Life of Women. Carlson (A. J.) Surg. & Gyn. Obs. (Chgo.) 1917, xxv, 283.

All evidence supports the view that some substance or hormone secreted by the islands of Langerhans into the blood is necessary for utilization of sugar by the tissues. This function is specific for the pancreas. Other endocrine organs may influence sugar metabolism in a superficial way by altering the sugar mobilization (adrenals, thyroid) or by increasing or decreasing the rate of oxidation in the body in general. The rest of the endocrine glands can not maintain the power of the tissues to oxidize sugar in the absence of the pancreas, and the hypo- or hyperactivity of other endocrine glands do not produce actual diabetes in the presence of normal pancreas. While the failure of the tissues to use sugar in the absence of the pancreas is the central and definite established fact, there are probably other primary defects involved in the development of acidosis, lipemia, increased metabolism, lowered resistance to infections, etc. All the evidence points to the view that true diabetes mellitus in man is primarily the result of pancreatic deficiency (islets). There is, at present, no organotherapy of diabetes, experimental or clinical.

There is, at present, no evidence of any specific relations of the endocrine functions of the pancreas to the gonads, male or female, or to menstruation, pregnancy and lactation. Absolute diabetes, induced after conception, leads to death of the fetus. Absolute diabetes probably renders conception impossible. Partial diabetes under careful dietary control permits of normal sex life of women (menstruation, normal pregnancy, normal child, lactation) and pregnancy under such conditions does not aggravate the diabetes. But in the absence of such dietary control the condition of pregnancy aggravates the diabetes in the mother, and uncontrolled diabetes in the mother is extremely injurious to the fetus. There is some evidence that in late stages of pregnancy the fetal pancreas may function for the mother.—Author's Summary.

(THYROID) Some Phases of the Differential Diagnosis of Exophthalmic Goiter. Plummer (W. A.) St. Paul Med. Jour. 1916, xviii, 297.

Although the article contains nothing strikingly new, it formulates and emphasizes some of the differential points between exophthalmic goiter and neurasthenia. Plummer considers the first salient and important symptoms to be increased appetite. This is constant and is in contrast to the poor and capricious appetite of the neurasthenic.

The fluctuation of symptoms in Graves' disease is typical. It is marked by a periodicity, measured in weeks and months while the symptoms of the neurasthenic vary from hour to hour and from day to day. The general demeanor of the ex-

ophthalmic goiter patient; the short, quick, nervous step; the bright, animated and at times prominent eyeball; the alertness and the intense restlessness, are in marked contrast to the languid, emotionless, complaining and introspective character of the neurotic.

The vasomotor disturbances are characterized by hyperhydrosis and warm hands, while in the neurasthenic they are hot flashes, cold sweats and cold hands. Bruits and thrills are present in 80 per cent of cases of Graves' disease. They are most intense over the superior thyroid vessels, whereas in non-hyperplastic goiters they are transmitted from the carotid and become more distinct as the clavicle is reached.—F. B. L.

(THYROID) Report of a Case of Adenocarcinoma of Thyroid. Campiche (P. S.) Cal. State Med. Jour. (San Francisco) 1916, xiv, 146.

The case report is one of metastatic adenocarcinoma of the thyroid with a comment on the relative benignity of this type. The author compares it with myeloid sarcoma. Hence this is the only instance in which a radical operation on metastic foci might be attempted with the hope of cure. These so called "metastatic colloid struma" (Kocher) produce colloid substances, and even though a radical thyroidectomy be performed cachexia strumipriva never arises when they are present.—F. B. L.

(THYROID) The Inconspicuous Everyday Forms of Thyroid Insufficiency. Harrower (H. R.) Calif. State Med. Jour. (San Francisco) 1916, xiv, 184.

While perhaps the long list of symptoms attributed to thyroid insufficiency might lead one to believe the thyroid is the cause of most of the vague complaints of patients, nevertheless Harrower's paper impresses the reader with the necessity of being watchful for signs of thyroid deficiency when the patient's ailments are seemingly those of neurasthenia. Among the symptoms and signs that he traces to thyroid insufficiency are nocturnal enuresis, headache, cold feet and hands, chilblains, psoriasis, prurigo, eczema, herpes, rheumatism, nasal and bronchial catarrh, rough skin, defective speech, enlarged tonsils and adenoids. "The most important single remedy in the asylum," he quotes from an alienist, "is thyroid extract." Many of those persons who "catch everything" are found to be in a low state of metabolic activity, the result of diminished thyroid secretion.

He advises the French method of administration. They give small doses of 0.01 gm. per day in three doses, given in alternate weeks. Pluriglandular therapy is recommended in obesity. Corpus luteum should be added at the climacteric.

Pituitary gland (whole) should be given with thyroid in children.—F. B. L.

(THYMUS) Enlargement of the Thymus Treated by the Roentgen Ray. Friedlander (A.) Am. Jour. Dis. Child., 1917, xiv, 41.

The author emphasizes the more frequent occurrence of enlarged thymus than is commonly realized and refers to Benjamin of Cincinnati, who found that out of 225 new cases in one year in his children's out-patient clinic, 19, or 8.4 per cent showed indisputable evidence of enlarged thymus. Quite a number of the cases occurred in babies suffering from congenital syphilis, but the author draws no conclusion from this observation.

Familial tendency has been noted, for in his recent cases four families had more than one child affected.

He calls attention to three definite symptoms of enlarged thymus, namely, dyspnea, continuous or remittent; suffocative attacks with cyanosis and stridor. The diagnostic physical signs are a detectable bulging mass in jugulum (more often absent than present) and enlargement of the area of normal thymus dullness or percussion. Definite information is afforded by the X-ray. Marked enlargement of the normal shadow, which is continuous with the heart shadow, is characteristic.

Out of 100 cases treated by the X-ray method there were four deaths as compared with seventeen deaths out of fifty cases treated by thymectomy (Parker).

The author uses Lange's technic, which he describes in detail.—M. B. G.

THYROID GLAND in Relation to Gynecology and Obstetrics. Marine (D.) Surg. Gyn. & Obs. (Chgo.) 1917, xxv, 272.

There is evidence in man of a thyroid sex gland interrelation recognizable in the female in association with the development of secondary sexual characters, with menstruation and pregnancy, and also in the male at puberty, but to a very slight degree. The meager evidence available would tend to indicate that the interstitial cells of the ovary, and perhaps also the adrenal cortex, play a major role in this relation in the female, as certainly the cells of Leydig do in the male.

The thyroid enlargement is of the nature of a work hypertrophy to stimulate metabolism identical in appearance so far as we know, different only in degree from that seen in simple goiter. Both of these reactions can be controlled and prevented either indirectly by giving iodine or directly by giving the iodine-containing hormone in physiological doses.—Author's Summary.

PINEAL GLAND, its Influence upon Growth and Differentiation with Particular Reference to Its Influence upon Prenatal Development. McCord (C. P.) Surg. Gyn. & Obs. (Chgo.) 1917, xxv, 250.

From the lack of unanimity in the literature any conclusions as to the details of pineal gland function must be made flexible rather than dogmatic. A survey of the available data leads to the following summary of internal secretion.

1. A clinical syndrome is to be associated with the disturbances of the function of the pineal gland. Because of the involution of the pineal at puberty, the constitutional manifestations of pineal pathology appear to be confined to pre-pubertial years. The essential characteristics, apart from pressure and neighborhood manifestations) are (a) early sexual development evidenced in the enlarged genitalia, pubic hair, general body hair, early change in voice; (b) precocious mental development, manifested in maturity of thought and speech; (c) general overgrowth of body to the extent that a child of six or seven years may have the appearance of a child near puberty.

2. The experimental extirpation of the pineal gland is surgically possible. The gland is not essential for the maintenance of life. The early symptoms of pinealectomy are attributable to severe brain injury. No changes attend the removal of the gland in adult animals. As to the effect of pinealectomy in young animals, Sarteschi, Foa and Horrax respectively state that the removal of the gland leads to precocity of development. Exner and Boese and Dandy report no changes after pinealectomy.

3. The administration of pineal substance to young animals is reported to hasten growth and sexual maturity. In unicellular organisms (paramoecia) pineal extracts increase the rate of reproduction to more than double that of controls. In larval forms (ranidae) both growth and differentiation are hastened as a result of pineal feeding.

4. The inference is allowable that the pineal gland is an organ of internal secretion whose functions, however, are of minor significance in the general activity of the endocrinous system.—Author's Summary.

PARATHYROID SYSTEM, its Relation to the Female Genital Apparatus. Pool (E. H.) Surg. Gyn. & Obs. (Chgo.) 1917, xxv, 260.

No direct relationship has been established between the parathyroids and the female sex organs; no morphological changes in the parathyroids have been noted during pregnancy; yet apparently there is a connection between the parathy-

roids and the sex processes in the female. Tetany, the clinical evidence of insufficient parathyroid function, is somewhat prone to occur in menstruation, pregnant and puerperal women, as well as patients suffering from gynecological diseases or who have undergone gynecological operations. The cause of maternal tetany is now referred to parathyroid insufficiency. The function of the parathyroids is apparently closely connected with calcium. There is no reason to believe that maternal tetany and lactation tetany are associated with calcium deficiency. Latent tetany, or a sub-tetanic condition, is much more common in pregnant and puerperal women than is usually assumed. Tetany in new-born infants, the offspring of tetanic mothers, is usually fatal within a short time after birth. In the treatment of maternal tetany the administration of calcium in large doses is followed by beneficial results in the great majority of cases.—Author's Summary.

(PITUITARY) The Relation of the Pituitary Gland to the Female Generative Organs; from the Experimental and Clinical Aspects. Goetsch (E.) Surg. Gyn. & Obs. (Chgo.) 1917, xxv, 229.

Perhaps between no two of the ductless glands is a closer interrelationship in function demonstrable than between the pituitary and the sex glands. There is abundant evidence available at the present time for believing that such a close association in function exists. We know from experiments in which the pituitary gland has been partially removed in dogs that a deficiency in pituitary secretion thus produced is followed by underdevelopment, genital inactivity and hypoplasia in young animals, and by impotence and sterility and retrogressive changes in the sex glands, together with adiposity in case the animals were adult at the time of operation. Conversely after primary alterations in the sex glands, as is seen in pregnancy or after castration, there is a consequent hyperplasia and hypertrophy of the pituitary gland. Overstimulation of young animals with the extract of pituitary anterior lobe is followed by overdevelopment and marked increased activity of the sex glands. Even histological evidences of such increased function are apparent, such as premature sex development evidenced by early and abundant ovulation in the female. It is the secretion of the anterior lobe of the pituitary which is responsible for these sex changes, whereas the posterior lobe secretion has an important function in regulating, certainly in part, carbohydrate metabolism, absence of this secretion being followed by a tendency to adiposity.

Clinical hyperpituitarism is well exemplified in the diseases, gigantism and acromegaly, now generally believed to be due to an overfunction of the anterior lobe of the pituitary

gland consequent upon adenomatous hyperplasia. In the early stages of these diseases we find an exaggerated sexual activity and libido, and in the late stages corresponding with pituitary involution and inactivity, a disappearance of the sexual function. The sex glands in this late stage show, histologically, atrophy and various forms of degeneration. Similarly inactivity and atrophy of the sex glands is seen in clinical cases of primary hypopituitarism, dependent upon pituitary underfunction following upon diseases of this gland or of its neighborhood compromising its function.

Pituitary extracts have gained wide usage in therapy. Thus "pituitrin" or "pituitary liquid," derived from the posterior lobe (together with pars intermedia) because of its stimulating action upon the smooth musculature of the uterus and bowel, is used very extensively and satisfactorily in obstetric practice and for the relief of abdominal distention and intestinal paresis following surgical operations in the abdomen or pelvis.

As a result of the facts learned from the experimental feeding of pituitary extracts, particularly of the anterior lobe, we should feel encouraged in our efforts to benefit clinical states dependent upon underfunction of this gland in the human. Thus, for example, a number of clinical cases showing among other symptoms, characteristic sexual disturbances (irregular menstruation, amenorrhea, sterility), dependent upon primary pituitary disease, have been so greatly benefited that there have been a return of menstruation and libido even when these had been absent for a considerable time.

It is probable that many clinical conditions showing genital aplasia, adiposity and underdevelopment and dependent upon changes in one or more of the ductless glands other than the pituitary, would be benefited by the feeding of pituitary extract in addition to the extract of the gland which is primarily involved. On the other hand, the feeding of extracts, such as thyroid and adrenal, combined with pituitary in clinical cases of pituitary diseases in which symptoms referable to these glands are present is advisable.—Author's Summary.

(THYROID) A Typical Case of Basedow's Disease. Tonsillitis as an Etiologic Factor. Hammill (R. C.) Med. Clin. of Chicago, 1916, ii, 85.

Hammill presents the case of a woman forty-one years old with a negative family history, who has had tonsillitis since the age of six. Enlargement of the thyroid was noticed at the age of eighteen, when it was much larger than at the present time. She had at that time puffiness of the eyes, shortness of breath, and was very nervous. Then the symptoms ceased up until at twenty-four she had another attack

and was afraid to walk because "her heart beat so hard." Ever since then any excitement has caused severe emotional strain. At the present time she has the symptoms of exophthalmos, Stellwag's positive, Moebius' negative, tremor of outstretched hand, perspiring freely under axilla, flushed skin around neck and over upper chest, marked dermographia, swelling of the isthmus and right lobe of the thyroid. Marked palpitation of the carotid. Blood pressure 150-78. Temperature normal, blood count normal. Pulse 115-125. Tonsils enlarged; from the right pus was ejected. Hammill thinks that the tonsils either became infected with a microorganism whose virulence varied from time to time or else they became a locus minoris resistentiae to microorganisms such as we are constantly taking into our mouths, and hence reinfected at frequent intervals. He thinks that tonsillar infection stimulates the thyroid in many cases, as it produces acute inflammatory rheumatism and chorea in others.—C. E. E.

SCLERODERMIA (The Cause of) Bydrage tot de Kennis van de aetiologie der sklerodermie. Nederl. Tijdschr. voor Geneesk. (Haarlem) Koopman (J.) 1917, ii. 55.

Description of a case of sclerodermia, complicated with a tuberculosis of the knee joint. A year after the first symptoms, the symptoms of an insufficiency of the adrenal system and still some months after a classical Addison's disease was observed.

An emulsion of the skin produced tuberculosis in the guinea pig. Application of the thyroid gland and of hypophysis had no result whatever.

In this case the author believes that sklerodermia has been caused by tuberculosis, and that the Addison's disease is simply an effect of the same cause.

As it is well known that tuberculosis may cause pluriglandular insufficiency and as it is absolutely certain that in many cases of sclerodermia the function of the thyroid gland or of the hypophysis is changed, the author suggests the idea that sclerodermia and insufficiency of the endocrine organs are both caused by a specific infection, and that in cases in which the organo-therapy has no success, this infection has not had an influence on these glands.—J. K.

(PARATHYROIDS) Relations between Epilepsy and Tetany. Bolten (G. C.) Geneeskundige Bladen (Haarlem) 1917, xix, 301.

Many authors have observed cases in which the patients showed epileptic symptoms as well as tetany, but there has never been described a case of epilepsy and tetany in which there was proof that both diseases had one common cause.

Bolten discusses these cases at length and comes to some very important conclusions which have a distinctly practical bearing.

Not all cases of tetany depend from the parathyroids. Especially in Austria and Russia there have been observed epidemics of tetany, which have most probably no relation with the parathyroid glands, but are caused by ergotin-intoxication. The tetany of children, however, is nearly always caused by insufficiency of the parathyroid glands. Epilepsy, too, shows very often no relation to the internal secretion. The traumatic epilepsy, the epilepsy in cases of tumors of the brain and the reflex-epilepsy have nothing to do with the endocrine organs. Only the "genuine" epilepsy is caused by insufficiency of the thyroid gland as is proved by the splendid effects Bolten has observed in administering fresh thyroid glands in cases of epilepsy.

Therefore, in cases of combination of epilepsy and tetany one has to examine carefully, whether the cause of these diseases is an insufficiency of the thyroid and parathyroid glands. Only in this case Bolten has observed very good results from rectal applications of fresh thyroid and parathyroid glands at the same time.

In other cases, however, not due to insufficiency of the thyroid-parathyroid system no effect can be expected from this treatment.

In the literature there is nothing to be found about this for the simple reason that in no case did the author investigate whether the tetany or the epilepsy really depended upon endocrine causes.—J. K.

(OVARY) Carcinomatous Ovarian Teratoma with Premature Puberty and Precocious Somatic Development. Harris (R. H.) Surg., Gyn. and Obst. (Chgo.) 1916, xxiv, 604.

The case of carcinomatous ovarian teratoma reported herewith is of special interest for the following reasons:

1. Malignant ovarian teratomata, including all solid teratomata, are rare; and those showing carcinomatous or sarcomatous areas are still fewer in number.

2. No other case reported as ovarian teratoma has been associated with precocious sexual and somatic development; although Fusino reports premature menstruation in a patient with a solid ovarian teratoma, and Askanazy has collected four cases of ovarian sarcoma, believing them to be cases of embryonal teratoma, in which there were in all cases genital hemorrhages, three times growth of pubic hair, twice mammary hypertrophy and twice abnormal height.

3. The patient was younger than in case of any of the published reports of ovarian teratoma excepting three cases

of malignant ovarian teratoma in girls fourteen years old and younger.

4. The growth of the tumor was associated with the beginning of puberty at five years of age and with rapid bodily development.

5. The tumor was a complex cysto-solid teratoma with definite adenocarcinomatous areas.

6. There has been no menstruation since the removal of the tumor, and no further precocious growth.

7. There was no discoverable recurrence when the patient was examined thirty months after removal of the tumor, a much longer time than the average freedom from recurrence.

The patient was a girl of five years and ten months. The family history presented three cases of carcinoma. The patient weighed six pounds when born, and grew normally until the age of four. The physical changes usually observed at puberty began to be noticed soon after the first menstrual period. The breasts grew larger, the areolae darkened, the pubic region became covered with dark brown hair, hair appeared in the axillae, and the whole body developed rapidly.

The growth of the ovarian tumor was well advanced by the time of the third menstrual period, seven months before operation, when its presence was discovered by the family physician. An inverted pear-shaped mass was then palpable slightly to the right of the median line of the lower abdomen. The examination was made on account of symptoms suggestive of appendicitis. The presence of the tumor apparently was not considered sufficiently important at that time to demand surgical consultation. As the tumor gradually increased in size, it caused a corresponding enlargement of the abdomen. Bodily movements, such as those involved in buttoning the shoes, became difficult to perform and caused discomfort. The patient no longer cared to play, and was more and more inclined to sit about and to rest with the head on a table or other support. She complained of being nauseated and her appetite became capricious. Her bowels moved regularly, except during the menstrual periods, when enemata were found necessary. During the last week before the removal of the tumor, the patient slept only two or three hours at a time, with intervals of wakefulness, when she groaned and seemed to be in pain.

There were no abnormal findings in the case except the signs of puberty, precocious somatic development, and the physical changes caused by the comparatively large size of the ovarian tumor. The bodily development was symmetrical.

Reference to the standards determined by Bowditch in an examination of 24,500 children attending school in or near

Boston, shows that the patient at five years and ten months was actually larger than the average girl nine years of age. She was 49.8 inches tall and weighed 58 pounds; while the average girl of nine is 49.39 inches tall, and weighs 57.07 pounds inclusive of clothing. Seaver gives the average height as 49.7 inches and the average net weight as 54.9 pounds for a girl of nine.

A laparotomy was performed, and the mass, which proved to be a tumor of the right ovary, was removed. It weighed 68 ounces, or about one-fourteenth the body weight of the patient. Microscopic examination showed areas of definite dermoid character, such as hair, sebaceous and sweat glands, fetal living tissue, etc. The larger part, however, presented the appearance of adeno-carcinoma.

The patient was examined twelve, eighteen, and thirty months after operation. She has been well, and has grown at a normal rate since removal of the tumor. There has been no menstruation since then.—E. N.

Relation of Glands of Internal Secretion to Female Pelvic Organs. Vest (C. W.) Am. Jour. Obst. (New York) 1916, lxxv. 366.

This paper, which is a brief resume of the gynecological relations of the internal secretions, is summarized by the author as follows:

There are definite conditions associated with the female pelvic organs, which are indicative of an abnormal condition of some of the glands of internal secretion. The hypophysis, thyroid, and ovary are intimately associated; that gland therapy is of value in cases of lactation atrophy of the uterus, in certain cases of amenorrhea, and in women at the menopause. It has been observed that the breasts react to changes in the pelvic organs when there is a disturbance in the internal secretions of the latter, as is evidenced by their accumulation of fat. Furthermore, they are often painful, and in certain cases of amenorrhea, after the ingestion of the luteum extract, they secrete an opaque, watery fluid. Finally, the author reports two instances of cessation of the menses, associated with an accumulation of fat, following an acute infection, thought to be measles, which had occurred early in menstrual life.—E. N.

(ADRENALIN) L'action de l'adrenaline sur le tractus digestif. (Action of Adrenalin on the Digestive Tract.) Loeper (M.) and Verpy (G.) C. r. Soc. de Biol. (Paris) 1917, lxxx, 703.

Intramuscular injection of one milligram of adrenalin in human subjects caused an increase in secretion of HCl in the stomach as well as augmentation and acceleration of the con-

tractions in the digestive tract. They suggest that there may be digestive syndromes originating from the adrenal.—F. A. H.

(PANCREAS) Spontaneous Diabetes in a Dog. Krumbhaar (E. B.) Jour. Exp. Med. (New York) 1916, xxiv, 361.

Krumbhaar reports a case of typical diabetes occurring spontaneously in a dog. The autopsy performed immediately after death showed the pancreas to be large, soft and with no signs of old or recent inflammation. Histologic examination, however, showed striking changes in the islands of Langerhans. Not only were these scarce but every island showed degeneration of one or more kinds. There was extreme hydropic degeneration and exhaustion of the granules involving both the alpha and beta cells but especially the latter. Some of the islands were replaced by fibrous tissue.

In addition this dog showed a sarcoma of the thymus.

J. R. G.

(DIABETES) The Effect of Exercise upon Carbohydrate Tolerance in Diabetes. Barringer (T. B.) Am. Jour. Med. Sci. (Phila.) 1916, cli, 181.

In speaking of the effect of exercise upon carbohydrate tolerance in diabetes, he reminds us that this tolerance is increased in the mild cases and decreased in the severer forms. Experimentally he gave patients dumb bell exercises one hour daily three times a week. In one mild case the patient whose tolerance was 150 grams of white bread daily, after eight months of such exercise, showed an increase of the tolerance to 270 grams. During the summer months the patient stopped these restricted exercises and led an active outdoor life, chopping trees and working with a pick. The tolerance decreased steadily so that by September it was 120. Resuming the exercises the patient was able to tolerate 190 grams by January.

In another case the tolerance was increased from 60 to 90 grams while in a third no such effect was noticed.—J. R. G.

(THYROID) The Alleged Detoxicating Power of the Thyroid Gland. Bassinger (H. R.) Jour. Infec. Diseases (Chgo.) 1917, xx, 131.

The author gives a good review of the work which has been done as regards the detoxicating power of the thyroid. Not being satisfied with previous results he has attempted to solve the problem by injecting a minimal, sub-minimal and repeated sub-minimal lethal doses of diphtheria toxin into the thyroid of a dog. In a second series of cases he used tetanus toxin. He finds that minimal lethal doses cause death more rapidly than in the control dog. Sub-minimal doses, that is,

about one tenth of the former, produce only the slightest symptoms of toxemia. The colloid in the glands was the same as in the controls. Repeated sub-minimal doses produced no hyperplasia nor increase of colloid. He concludes that the thyroid has no detoxicating properties that can be demonstrated by the injection of diphtheria or tetanus toxin into the thyroid. Microscopic examination showed no increase in colloid, repeated injections caused some resorption of colloid but no active hyperplasia.—J. R. G.

(DIABETES) The Influence of Acidosis upon Hyperglycemia in Diabetes. Epstein (A. A.) and Felsen (J.) Am. Jour. Med. Sci. (Phila.) 1917, cliii, 58.

Acidosis as known manifests itself in a variety of ways. (1) By increasing the acidity of the urine, (2) By increased hydrogen ion concentration of the blood serum, (3) Diminished combining power of the serum for carbon dioxide and hence (4) Reduced carbon dioxide tension in the alveolar air, (5) Increased ammonia output in the urine and the elimination of ketone bodies.

Recent observers have shown that acidosis not only is associated with diabetes but in itself may produce glycosuria. This is also true in acid poisoning and again after removal of the pancreas sodium carbonate when given diminishes glycosuria. The acidosis may be affected in two ways: (a) by action upon the liver and muscles immobilizing glycogen and (b) it may interfere with renal elimination.

The hunger treatment in diabetes shows that some cases improve remarkably; others develop a severe acidosis. The author studied four cases and showed that (1) the withdrawal of food from certain cases of diabetes provokes and aggravates an acidosis, (2) this acidosis causes an increase in blood sugar content, (3) a liberal but judicious administration of carbohydrates may control the acidosis provoked by carbohydrate withdrawal or complete fasting and lead to general amelioration of the symptoms, (4) a progressive rise in the blood sugar content associated with a gradual fall in the alveolar carbon dioxide is indicative of impending coma.

J. R. G.

(INTESTINE) Has Secretin a Therapeutic Value? Carlson (A. J.), Lebensohn (J. E.) and Pearlman (S. J.) J. A. M. A. (Chgo.) 1916, lxvi, 178.

Secretin is the product of the action of the acid duodenal contents upon the duodenal mucosa. It can be prepared artificially by mascerating the duodenal mucosa in a 0.4 per cent hydrochloric acid solution, neutralizing the boiling mixture and filtering. A few cubic centimeters of the filtrate after

injection invariably produces a powerful secretion of the pancreatic juice. Secretin excites not only the pancreas but also the liver and intestinal mucosa. It stimulates markedly the flow of bile and the succus entericus. Remarkable it is that the pancreas is not fatigued but has been observed to maintain undiminished flow for eight hours. Secretin seems to be a specific substance much like adrenin, both being nonspecific in distribution, relatively simple in composition, of low molecular weight and subject to rapid oxidation.

In diabetes, it has been emplowed with conflicting results. It is apparently of no definite value. Likewise in digestive disturbances and in a variety of ailments it has been tried but with no definite basis for its use.

Direct introduction of secretin even in large quantities into the intestine of an anesthetized dog is with no effect. It apparently cannot pass the digestive tract. Experiments with human gastric juice also prove that secretin is destroyed. Experiments upon dogs with duodenal fistulae reveal no specific results from the administration of secretin by mouth. The authors then examined two proprietary preparations, Secretogen and Duodenin. These also were found to be without effect in their experiments.

The authors conclude that secretin is of value only when given intravenously, and its action is transient like that of adrenin.—J. R. G.

(DIABETES) Clinical Significance of Glucose Nitrogen in Diabetes Mellitus. Janney (N. W.) Am. Jour. Med. Sci. (Phila.) 1917, cliii, 44.

By means of improved experimental methods the writer establishes the fact that in the fasting subject, the glucose nitrogen ratio of severe diabetes mellitus is about 3.4 to 1. The glucose-nitrogen ratio is therefore to be regarded as a definite index of the severity of the disease. In association with other factors the ratio is a valuable prognostic sign.

J. R. G.

(DIABETES) Observation on the Starvation Treatment of Diabetes. Martin (C. F.) and Mason (E. A.) Am. Jour. Med. Sci. (Phila.) 1917, cliii, 50.

In offering 100 grams of glucose to a normal person, there is of course an increase in blood sugar but this drops below normal in from two to three hours. In diabetes the rise is sustained much longer. This very slow decline suggests possibly a kidney block. While it is not an absolutely established point, considerable evidence suggests the importance of kidney block in these conditions. Thus an insidious

and progressive diabetes may be entirely overlooked. Experience shows that the best time to make estimates of blood sugar is two hours after the meals.

In some cases test diets repeated at short intervals show great variations in the patient's tolerance. As regards acidosis, the ferric chloride reaction is sometimes absent in the presence of acidosis. Starvation in an ordinary individual results in acidosis, but in a diabetic usually the reverse. However, in the latter acidosis may at times be initiated by hunger.—J. R. G.

(PITUITRIN) The Action of Pituitrin upon the Surviving Human Uterus. Charteris (F. G.) Glasgow Med. Jour. 1917, lxxxvii, 65.

The author criticizes much of the work in animal experimentation by saying that drugs are too often given in toxic doses and secondly that animals are selected not for their resemblance to the human but for the ease of experimentation. Accordingly, he used strips of human uterine tissue about one inch in length and one eighth of an inch in thickness. The material was obtained from non-pregnant tissue, from tissue removed after early abortion and from tissue removed by Caesarean section at full term. These strips were suspended in balanced salt solutions and curves taken indicative of their contraction. There was no difference in the response to pituitrin of the pregnant and non-pregnant uterus. Both responded by increased activity. Contractions became more numerous, the tonus was markedly increased and the individual contraction shorter with more rapid relaxation. The action is prompt, occurring within a minute and lasting several minutes. Neither adrenin, ergotine, fluid extract of ergot, nor quinine produced the same prompt effect. In these experiments added to the solution made a concentration of about one to five thousand.—J. R. G.

(PITUITARY) A Case of Diabetes Insipidus with Peculiar Necropsy Findings in the Posterior Lobe of the Pituitary Body. Weber (F. P.) and Schmidt (H.) Am. Jour. Med. Sci. (Phila.) 1916, clii, 892.

The relation of the pituitary to polyuria has long been known and indeed some authors have described polyuria in cases where the lesion did not directly involve the pituitary but was simply in that region. These authors describe a very interesting case of a woman 73 years of age. Polyuria started suddenly, following the removal of a lymph node in the neck. Upon admission to the hospital two years later the patient was found to be suffering from tuberculosis. She was pass-

ing ten liters of urine daily, blood pressure was 90 and the Wassermann and eye-ground examinations were negative.

Post-mortem showed the usual findings of miliary tuberculosis except for the pituitary. Here the pars posterior (pars nervosa) was relatively enlarged over the anterior lobe (pars glandularis). The posterior lobe almost enclosed the anterior lobe and contained large clumps of granular cells rather large and with small nuclei which stained deeply with hemotoxylin. The cytoplasm was granular and Sudan III showed these granules to be droplets of lipoid substance.

J. R. G.

(KIDNEY) Renal Glycosuria. Murlin (J. R.) and Niles (W. L.) Am. Jour. Med. Sci. (Phila.) 1917, cliii, 79.

The authors describe a case of renal diabetes, with glycosuria and normal glycemia, relatively independent of diet. The case was of interest in that only one day of hunger was needed to clear the sugar from the urine.—J. R. G.

(PANCREAS) A Contribution to the Study of Pancreas Intoxication. Goodpasture (E. W.) Jour. Exp. Med. (New York) 1917, xxv, 277.

This study was undertaken with the idea of purifying as far as possible the toxic part of the autolysing gland. It was found that the fresh pancreas extract in salt solution is toxic and when injected intravenously produces symptoms of poisoning analogous to those resulting from the duodenal loop fluid and other toxic materials of protein nature. As little trypsin could be present in a gland rapidly extracted, it seemed probable that the toxic agent was some other substance. The beta nucleoprotein fraction of the gland seemed toxic and produced reactions identical with those following the salt solution extract. Further studies showed this toxic agent to be thermostabile. It is destroyed by autolysis but can be obtained in a gland which had autolyzed twenty-four hours. It is probably protein in character. Intravenous injection of 0.05 to 0.1 grams per kilo is usually fatal and elicits symptoms in dogs comparable to those of hemorrhagic necrosis of the pancreas. After autolysis of the dog's pancreas this toxic protein and guanylic acid may be separated and obtained in relatively pure form.—J. R. G.

(PITUITARY) Diabetes Insipidus and the Hypophysis. Von Meyenburg (H.) and Mason (E. A.) Beitrage path. anat. u. allg. path. 1916, lxi, 550.

They remind us that the majority of evidence points to the involvement of the pars posterior in polyuria and polydypsia. They quote two cases. In the first, a very marked

case, autopsy showed a small tumor of the optic chiasma. Histologic examination proved the tumor and also the hypophysis to be tuberculous. In a second case a man 21 years old with severe diabetes insipidus, frontal headache, abducens and oculomotor paralysis, died eight months after the onset of the symptoms. Autopsy showed a malignant tumor at the base of the skull in the region of the hypophysis. Both cases showed especial involvement of the pars posterior but he believes that the best explanation is not a hypo- or a hyperfunctioning of one part but a dys-function of the entire gland.—J. R. G.

(THYMUS) Syphilitic Disease of the Thymus in Infants and the Mode of Origin of the Dubois Abscesses. Oliver (J.) Amer. Jour. Dis. Child. (Chgo.) 1917, xiii, 158.

Abscess-like cavities in the thymus were first adequately described by Dubois in 1850. These cavities are characterized by a lining of stratified squamous epithelium and contents that are puriform in appearance. There are three theories as to their origin: that they are derived from the Hassall bodies; that they come from the primary cavity of the developing thymus; and that they arise by a necrosis of the medullary tissue. In addition to the "abscesses," in many instances there is a preponderance of reticulum and a disappearance of the lymphocytes in the thymus as a whole. Oliver reports a case in which the origin of the cavities by a cystic dilatation and coalescence of the Hassall bodies appeared to be unquestionable. The syphilitic etiology of this condition is universally recognized, although Oliver was unable to demonstrate spirochetes in the tissues of the case reported, probably as a result of improper fixation.—J. P. S.

THYMUS Disease in Children. With Report of a Case of Thymus Hypertrophy. Sheffield (H. B.) Pediatrics, 1917, xxix, 5.

Hypoplasia of the thymus and the associated hypothyroidism, "produces not only arrest of growth and frailty of bones and general debility, but also lowered mental capacity." There are three groups of cases associated with hyperplasia of the thymus: In the first, hyperplasia of the thymus with the accompanying increased activity of the thyroid, may cause the clinical picture of exophthalmic goiter. In the second group, the child shows no definite manifestations of any pathological condition, but may die without any apparent reason as a result of some slight cause, such as an injection of serum, narcosis or a slight operation. In the third group, an enlarged thymus is demonstrable on percussion and is associated with enlarged lymph glands elsewhere in the body. These children suffer from so-called thymic asthma, and may

die suddenly during a paroxysm of asphyxia. The case reported very briefly by the author is of this type.—J. P. S.

(PITUITARY) Alleged Antitoxic Action of Pituitary Extracts. Houssay (B. A.) and Giusti (L.) Semana Médica (Bs. Aires) 1916, xxiii, 559.

The pituitary body extracts have no antitoxic properties against veratrin, strychnin and morphin.—G. P. G.

MENSTRUATION, Cholesterinemia Variations during. Gonalons (G. P.) Semana Médica (Bs. Aires) 1916, xxiii, 639.

The author recorded the findings in twenty-seven complete menstrual cycles. They show that the cholesterin content of the blood rises abruptly five, six or seven days before the menses and then gradually declines a little. It rises again as the menses become established, keeping at this same level, somewhat below the early peak, until the close of the menses and then gradually dropping back to the ordinary level where it remains till it runs up abruptly anew from five to seven days before the onset of the next menses. One woman with exophthalmic goiter and one with postpuerperal amenorrhea showed this same curve of the cholesterinemia although there was no uterine discharge and another with a probable depressed ovary gave an irregular curve. The author believes that this curve is not due to the internal secretion of the corpus luteum alone.—G. P. G.

PITUITARY Body. Esposel (F.) Revista dos Cursos de la Facultad de Medicina (Porto Alegre, Brazil) 1917, iii, 28.

A general summary of the knowledge of this ductless gland.—B. A. H.

(MAMMA) Chronic Inflammation of the Mamma and Treatment with Mammary Extracts. Navarro (A.) Anales de la Facultad de Medicina de Montevideo (Uruguay) 1917, i,, 323.

Navarro obtained the cure of four patients by mammary organotherapy.—B. A. H.

PITUITARY, Tumor of the. Adiposo-genital Syndrome. Ricaldoni (A.) Anales de la Facultad de Medicina de Montevideo (Uruguay) 1917, ii, 328.

The author describes the first case that has appeared in the Uruguaian medical literature. There were present absolute blindness, headache and adiposity. The height was 172 cm. and the weight 75 kg. Amenorrhea has persisted during the six years since the incidence of disease. X-ray of sella showed a greatly enlarged hypophysis. Radiotherapy had no effect.—B. A. H.

(THYROID) Tuberculosis and Hypothyroidism Co-existent. Albina (E.) Rev. de la Assoc. Med. Argent. (Bs. Aires) 1917, xxvi, 967.

Girl, fourteen years of age, with profuse menses lasting eight days; temperature reaching 38 degrees C, perspiration often profuse, severe pains in the ankle and in the hand. Infiltration tuberculosis of the vertex of the lungs. As the treatment by sodium salicylate was unsuccessful she was given thyroid and the following menstruations were normal and the other symptoms disappeared.—B. A. H.

(MAMMA) A Remarkable Hypertrophy of the Breasts. Novaro (R.) Anales del Instituto Bodelo de Clinica Med. (Bs. Aires) 1915, i, 61.

I. S. A., twenty years old, single, with irregularity of menses and sometimes severe menorrhagia. Hypertrophy of the breasts had begun six months before she was examined. It increased during the menses. Constipation, headache and insomnia were present. The breasts reached almost to the pubis; the nipples had nearly disappeared; the diameter of the right areola was 11 cms and of the left 13 cms. The Wassermann reaction was positive. After operation, the left breast was found to weigh 6700 gms and the right 5,900 gms. Novaro believes that this remarkable mammary hypertrophy is due to abnormal functioning of the ovary.—G. P. G.

(ADRENALS) Cortico-adrenal Virilism. Guemes (A.) Semana Médica (Bs. Aires) 1917, xxiv, 207.

Woman, ... years old, bald, with a dense beard and moustache; amenorrhea of three years; gained twelve kgrs. in six months; pigmentation of the face.

At autopsy it was observed that the right adrenal was hypertrophic, weighing 141 gms. The tumor was made up of spongiocyte cells and there were metastatic cells in the liver. The cholesterol content of the adrenals was 11 per cent. No adrenin content was detected.—G. P. G.

(THYROID) Pathogenesis of the American Trypanosomiasis. Chagas (C.) Memorias do Instituto Osvaldo Cruz. Rio de Janeiro (Brazil) 1916, viii, Fac. ii, 5.

A general summary of our knowledge of this disease, discovered by the author and produced by the Trypanosom cruziei.

This disease begins, according to Chagas, by an acute state lasting thirty days, more or less, after which the Trypanosomes disappear from the blood and the disease becomes chronic. The evident symptoms are: myocarditis and ar-

rhythmia, injuries of the nerves, goiter, etc. Chagas modifies his previous classification of the clinical forms, leaving only the cardiac, the nervous and adrenal forms, and suppresses the pseudo-myxedematous and myxedematous forms and the chronic with acute exacerbations because he has found that these are mixed with the aforementioned forms.

He believes that the infantilism he has observed is different from cretinism. He has found cysts of leismaniform corpuscles in the heart, muscles, nervous system, thyroids, adrenals and testicles. Chagas discusses the water theory of endemic goiter and offers some objections to the theory, because he thinks that it is probable that Trypanosomiasis exists in assocation with the other, endemic, form of goiter.—B.A.H.

(GONADS) Genito-Glandular Dystrophy. Souza (O. de) and Castro (Aloisio de). Annaes da Policlinica General Do Rio de Janeiro (Brazil) 1916, i, 9, 121; 1917, ii, 5, 79.

Souza and Castro offer an excellent study of the diseases produced by endocrine dysfunctioning in which the main symptoms are atrophy of the gonads and general trophic alterations. Their observations comprise twenty cases. The common link of them is atrophy of the sexual organs. Three of the cases had tumors of the pituitary body (one is Ricaldoni's case). The authors believe that the principal factor in these cases is functioning of the gonads. They classified their cases in these divisions: (A) Sexual-Gland Dystrophy of an infantile type. (B) Sexual-Gland Dystrophy of gerodermic type. (C) Genital Dystrophy of eunuchoid type. (D) Sexual Dystrophy of adiposo-genital type. (E) Associated types of genital dystrophy (pluriglandular syndromes).

Their other classification is commented on by Dr. Houssay. Simple Types: Where there are genital disturbances alone. Infantile Types: Which term they say, with reason, must be limited to the patients who retain infantile characteristics till puberty or later. The authors take issue with those who believe that the genital insufficiency is able to produce the infantilism. A given cause they say could produce both the somatic infantilism and the arrest of development of the sexual organs. Also, experimentation has given us no reason to believe that removal of the gonads will produce arrest of somatic development. Gerodermic and Eunuchism Type: Souza and Castro group, reasonably according to us, those cases in which are observed singly or together the senile type of skin, alterations in growth and distribution of the hair, adiposity of breasts and hips, abdominal adiposity of the eunuch and sometimes the thin type of eunuchism. Since the injuries of the pituitary often produce indifferentiable syndrome with alterations of the sexual organs, Souza

and Castro believe that Frohlich's syndrome is a genito-glandular dystrophy due to pituitary tumor. They affirm the manifestly hazardous hypothesis, that injury to the sexual glands might produce the disorders secondary to the pituitary body. This theory is opposed by the experimental fact that sexual atrophy is produced by removal of the pituitary body. Associated Types: The authors group all those cases known by the term of pluriglandular syndromes and most probably due to disorders of the internal secretory activity of the gonads.—B. A. H.

(THYROID) Chronic Thyroid Rheumatism. Servetti Larraya (J). Revista Médica del Uruguay, 1916, xix, 829.

Servetti Larraya gives a summary of the etio-pathogeny of this condition and a discussion of the literature pertaining to it, followed by a description of his case. A. L., man, forty-two years old, without syphilitic history. (Gonorrhea was not inquired about.) For the past four years has had painful (gouty) attacks in several joints, with deformities and rigidity. All medication employed was unsuccessful. Then Dr. Servetti Larraya gave him thyroidine (Tyrénine Grémy) 0.02 cgms. daily during eight days. After a week's interim thyroid treatment was resumed for twenty-seven days, 0.04 cgms. daily. Treatment was then discontinued two months, but a new attack having occurred it was necessary again to give him thyroidine during twenty-four days. The patient again improved.—G. P. G.

EXOPHTHALMIC GOITER, The Treatment of, by Injections of Boiling Water. Ceballos (A.) and Bacigalupo (G.) Rev. de la Asoc. Méd. Argent. 1917, xxvii, 236.

The authors give the remote consequences of the treatment of six patients by Porter's method. Two of the patients were men and the remainder women. As many as thirty injections were administered. Some of their patients were observed for two years, the others for one year following the treatment. They noted a decrease in the size of the thyroid. In three patients, after two years of treatment, the pulse rate diminishd from 130 to 100 beats per minute. The exophthalmos was unaltered. The subjective symptoms were decreased by the treatment and the patients felt better.

Two patients were presented at one of the meetings of the Asoc. Med. Argent., but we have not seen all the improvements of which the authors speak.—G. P. G.

EXOPHTHALMIC GOITER. Basedow's Disease. Celesia (A. F.) Thesis of Professorship of Faculty of Medicine of Buenos Aires, 1916.

The author gives a fairly complete study of the literature of the subject. He claims much for his treatment of this disease on the results obtained in one mild case of exophthalmic goiter, in which he used a homo-graft of the ovary. In another case he made a testicular graft in a pederast. The grafts were successful. (Manuscript read before the Society of Surgeons of Buenos Aires, July 14, 1915.)—G. P. G.

(OVARY) Etio-pathogenesis of Uterine Fibromata. Piccardo (T. J.) La Prensa Médica Argentina (Bs. Aires) 1916, iii, 65.

Piccardo is convinced that excessive function of the ovaries (hyperovarism) is directly concerned in the etiology of uterine fibromata. He promises a later paper concerning the histology of the ovaries removed during their operations.

He has found, as have other observers, that in patients with these tumors, the ovaries are increased in size, sometimes being as large as a plum, with elongation of the thrompes. He believes that these fibromyoma are produced by a hyperactivity of the ovary because of the size of the ovaries, the elongation of thrompes and the profuse menses He believes also, that this ovarian activity can begin in the early states of puberty. In these cases the tumor remains single, or as a nucleus and does not occupy the whole uterus, as often occurs in the latter states of feminine sexual life when the tumors become numerous. He suggests antagonistic organotherapy as treatment, the thyroid gland being his choice.—G. P. G.

(PITUITARY) Hypopituitarism in a Boy with Positive Wassermann. Cockayne (E. A.) Brit. Jour. Dis. Child. 1917, xiv, 52.

This patient was 9 years old and had appeared normal, healthy and intelligent until 2 years ago, when he complained of severe headaches, became languid; later muscular weakness was noticed. Became fat 6 months ago. He was dull, apathetic and showed continual tremors of hands and legs. He talked intelligently for a time and then lapsed into baby talk, speech becoming slurred and indistinct. The gait became unsteady and the knee jerks exaggerated; pupils: right reacted to light and accommodation, left reacted to light slightly and sluggishly. Both discs were chalky white with optic atrophy. The forehead was bulging. Marked deposit of fat occurred all over body. The testicles were small and the penis was very small.

Two Wassermanns were positive.—M. B. G.

PITUITARY Gland and Idiocy. Cornell, (W. B.) Medical Ass'n, Greater New York, Oct. 15, 1917.

The speaker presented a case of a hyperactive idiot, 7 years old, but who measured up to less than 3 years mentally. An x-ray picture of the head, which was markedly microcephalic, showed the anterior clinoid process almost doubled on itself and encroaching on the pituitary gland. Treatment with pituitary extract resulted in some slight improvement.

M. B. G.

DUCTLESS GLANDS, Practical Experiences With. Black (S) N. Y. State Jour Med. 1917, xvii, 125.

The writer's experience is very different from that of Dana and Berkeley in the treatment of feeble-minded children with pineal substance. He has not found a single case where he could state positively that the improvement was due to this medication.

He also thinks that the use of the parathyroids in paralysis agitans and tetany has been made more of lately than is warranted. In 9 old persons with typical paralysis agitans absolutely no results could be attributed to the treatment with this gland. He has not used it in a genuine case of tetany.

In obesity, Black recommends the use of thyroid extract in large doses, carefully watching the blood pressure and heart. He has given as much as 30 grains a day in conjunction with the Bergonie treatment.

He refers to a case of goitre that disappeared entirely with adrenalin chloride solution 1-1000, ten drops three times a day in water. Various combinations of hormones as ovary plus adrenal or pituitary, adrenal and ovary worked no better in his hands than the adrenals alone. Recurrences he found to be common.

In absolute contradiction to many experts, he believes that most of the conclusions as to the relationship between thyroid hormone and diabetes to be theoretical only, and from practical experience thinks it is a good plan to give diabetics thyroid. He refers to a marked case in which 30 grains of thyroid per day were given for several weeks, keeping down the sugar in the urine and the woman appearing stronger.

In cases of rickets, he considers the administration of calcium by mouth to be superior to that of thymus.

The reviewer feels that the value of this paper would have materially increased had the author included case histories and statistics to prove his views, many of which are at variance with those held by other observers and investigators. In their present form, they are at best but broad statements.

M. B. G.

MONGOLIAN IDIOCY, Etiology of. Herrman (C.), Arch. Ped. 1917, xxxiv, 494.

The author concludes that there is no positive evidence that worry, emotional shock, illness during pregnancy or congenital syphilis are important or essential factors in the causation of Mongolian idiocy. The evidence that Mongolian imbecility is a unit character and recessive, although not conclusive, is certainly suggestive.

He believes that distinct manifestations of disturbed function of the endocrine organs are not present in Mongolian imbeciles and post-mortem examinations have not shown any characteristic changes in the thyroid, thymus or supra renals. The administration of extracts of these glands in this disorder has not been followed by marked improvement.

M. B. G.

(PITUITARY TESTIS) Dystrophia Adiposa Genitalis with Congenital Lues. Langmead (F.) Brit. J. Child Dis., 1917, xiv, 55.

The author describes a case in a boy of 15 years. He did not walk until the age of 3 years and could not speak distinctly until 4 years of age. He was stunted, obese and feminine in build and his mentality measured up to about 7 years. The external genitals gave an appearance of a feminine character because the scrotum was divided by a deep groove but not by an actual cleavage; the penis was small and the testicles rudimentary. Luetic stigmata were shown by eyes, Hutchison teeth and scars about angles of mouth. X-ray showed small pituitary fossa and prominence of posterior clinoid process. The sugar content in the blood was about normal. The father died of general paralysis at 45; the mother had Tabes Dorsalis.

(From "La Pediatria." May, 1917.)

(PITUITARY) Su tre sogetti adenoidei con feminilismo ipofisario. Citelli (S.) e Caliceti (P.) La Pediatria, 1917, xxv, 278.

The authors found three cases of hypophyseal feminism in three soldiers, who had had adenoids in their youth. Through neglect their mental development was considerably reduced.

Skeleton and genitalia were normal, so that they are not eunucoids. Hypothricosis, delicate skin, development of the mammae, distribution of the hair on the pubis and sexual frigidity show hypophysary type of feminism.

X-ray examination shows absence of thymus and of the cranio-pharyngeal canal; no visible alteration of the hypophysis, so that it must be distrophy of the gland brought about by the adenoids (?). All three are very sensitive to hypodermics of "endo-ipofisina."

The absence of thymus and the lymphatism shows that their causative action of the syndrome, when present in cases like these, is about nil. G. V.

(THYMUS) Grave osteo-porosi Infantile Associata a sclerosi del timo. (Lansarini.) La Pediatria, 1917, xxv, 302.

A girl 26 months old with distrophy of the bones died of bronchitis. The post-mortem examination showed increase of weight of all the endocrine glands; osteo-porosis of all the bones; precocious involution of the thymus with sclerosis and sclerosis of the adrenals. G. V.

(PITUITRIN) La prova dell 'ipofisi nelle malattie delle ghiandole a secrezione interna. (Porak) La Pediatria, 1917, xxv, 499.

The reaction of normal individuals to hypodermics of pituitary is widely different from the reaction shown by those sick with diseases related to the endocrine function. G. V.

THERAPEUTIC EXPERIENCES

(PITUITARY) The Present Status of Pituitary Extract in Labor. Mundell (J. J.) J. A. M. A. (Chgo.) 1917, lxviii, 1601.

Mundell states that pituitary extract should be given only late in the second stage of labor, when the pains have become slow and weak, owing to uterine inertia, with a normal presentation, a ruptured bag of waters, a fully dilated cervix, and the head moulded and through the brim just above a relaxed perineum.

For 1916 (1914 statistics reported, Amer. Jour. Obstet. 1916, xxvii, 306) he reports 1293 cases, with a ruptured uterus in 12 cases (1 in every 106), 34 fetal deaths (1 in every 38), and 41 cases of asphyxia pallida (1 in every 32).—F. C. P.

(TESTES) Sterility Studies with Particular Reference to Weak Spermatozoa: Diagnosis and Treatment. Lespinasse (V. D.) J. A. M. A. (Chgo.) 1917, lxviii, 345.

The author divides the subject of sterility into five groups, viz: (1) obstruction in the sexual tract of the male, and (2) the female; (3) absolute failure of, or imperfect development of, essential male elements, or (4) of the essential female elements. (5) alterations in the secretions of the female sexual tract, so that her secretions are destructive to the life of the spermatozoa. The study is devoted chiefly to group three and the spermatozoa were examined for motility, size, shape, and staining reactions. A few cases with no obstructive lesions and with weak or imperfectly developed spermatozoa were treated with desiccated anterior lobe of pituitary and suprarenal cortex with good results. The remainder of the paper deals chiefly with group five and is not of particular interest from an endocrinologic viewpoint.—F. C. P.

(PINEAL) The Vineland Experience with Pineal Gland Extract. Goddard (H. H.) J. A. M. A. (Chgo.) 1917, lxviii, 1340.

Goddard makes a brief additional report of the work with pineal gland extract described in collaboration with Cornell (Med. Rec. (N. Y.) 5-10-13) and concludes, "It is thus seen that the Vineland experience, as far as it goes, is wholly negative."—F. C. P.

(OVARY, PLACENTA) Ovarian and Placental Extracts, Their Preparation and Standardization. Morley (W. H.) Surg. Gyn. and Obs. (Chgo.) 1917, xxv, 234.

A more uniform method of preparing extracts must be instituted. Some method for the standardization of these ex-

tracts must be discovered, in order to facilitate the comparison of the results of the different laboratory workers and clinicians. Many results obtained in the laboratory or in the clinic are due to the faulty preparation of extracts. The isolation of the active principles of the ovary and the placenta will clear up many, if not all, of these mooted points.—Author's Summary.

PITUITARY Extract in Obstetrics. Kinnear (J. A.) Canad. Pract. and Rev.. 1916, xli, 141.

Kinnear discusses the use of pituitary extract for the following indications:

(1) To Induce Labor—For this purpose the author considers pituitary unsatisfactory, preferring the use of bougies. From the latter he has never seen any bad effects. With pituitary, on the other hand, the patient experienced labor-like pains lasting perhaps an hour, then disappearing.

(2) In the First Stage of Labor—Kinnear says he has had both good and bad results in administering pituitary when the cervix is slow in dilating, as in an occipito-posterior position. He speaks of the danger to the child when the drug is used at this stage. The child's circulation is affected, so that it is sometimes still born, or may die of cerebral hemorrhage.

(3) In the Second Stage of Labor—It is in this condition that the best results are obtained, especially in multiparae. The method is most satisfactory when the child is born within a few minutes after the administration of the extract. Bad results may be obtained if the baby is delivered after the effect of the pituitary has worn off.

(4) In Cases of Slight Contraction of the Brim, So That the Head Sticks Above the Latter—If there is doubt about the head's coming through, the pituitary should not be given.

(5) In Cases of Placenta Previa and Post-Partum Hemorrhage—Here Kinnear's experience has been favorable. The placenta usually soon becomes detached. For hemorrhage the author usually uses ergot hypodermically, but where pituitary has been employed, it has quickly brought about uterine contraction and cessation of the bleeding.

(PLACENTA) The Use of Desiccated Placenta, with Special Reference to the Vomiting of Pregnancy. Cary (E.) Surg., Gyn. and Obst. (Chgo.) 1917, xxv, 206.

The theory on which Cary suggests the use of placental extract is based primarily on the work of Loeb, who in 1909 showed that the corpus luteum sensitizes the endometrium for the reception of the fertilized ovum. This action is the lowering of the resistance of the host to this foreign protein

(the ovum), thus making it possible for it to exist and not be absorbed. Now that the ovum is imbedded and growing, a relative immunity must be established by the pregnant woman against the products of conception.

The growing ovum acts as an antigen and stimulates the host to the formation of anti-bodies. This is in accordance with Ehrlich's theory of immunity with which we are all more or less familiar.

A. H. Curtis demonstrated the death and absorption of living ova in the uterus of the guinea pig and the rabbit, following the subcutaneous injection of placental extract. The results of his experiments may be explained by the fact that the injection of placental extract increases the resistance or raises the immunity of the host to such a degree that the existing balance is altered, causing death and lysis. Even in older pregnancies the action is sufficiently strong to cause death of the mature fetus and resulting still-birth.

Cary advises desiccated placental extract in the vomiting of pregnancy because (1) if the condition is due to a lowered immunity of the host to the growth of the syncytium, as seems probable by the work of Acconci, it may stimulate by acting as an antigen. The work of Curtis would also bear this out. (2) If the proteolytic ferment is lower than normal, as demonstrated by the negative Abderhalden reaction, it may increase the ferment content of the blood. (3) The placenta may be a gland of internal secretion, and it may increase the action of the thyroid and adrenals, and by so doing hasten the oxidation of partial protein split-products being thrown into the circulation.

Cary has collected thirteen cases of vomiting of pregnancy, which have occurred at different periods during gestation. One or two of these developing later in pregnancy, as they did, might have developed into the pernicious type had they been allowed to continue. Of these thirteen cases two were lost sight of. Of the remainder, seven stopped vomiting within a day or two and the nausea soon disappeared. Two improved and remained fairly free from nausea, although the administration of the extract had to be continued over a longer period of time. In the remaining two cases the results were not satisfactory; one was definitely neurotic.

At the author's suggestion Dr. De Lee has used the extract in six cases, with good results in three, and varying success in the remainder. He has also used it in two cases of urticaria of pregnancy, from which prompt and lasting relief was obtained.—E. N.

ORGANOTHERAPY in Gynecology. Block (F. B.) and Llewellyn (T. H.) Am. J. Obst. (New York) 1917, lxxv, 357.

This paper is a report of the experience of the authors in the treatment of various gynecological disorders with corpus luteum extract, thyroid, and pituitary. The most useful extract they have employed is, in their opinion, that of corpus luteum. They consider that the extract made from the ovary of the cow and that of the sow are of equal potency. They see no necessity for the large dosage which some have recommended, most of their own successful results having been obtained with small doses. They divide the cases treated with corpus luteum into four groups, as follows: (1) Hyposecretion of the ovary due to pelvic inflammatory disease, (2) Natural menopause, (3) Surgical menopause, (4) Functional insufficiency of the ovary.

In the first group, the ultimate results have shown that eight patients were markedly improved and have remained free from the symptoms of which they complained at the inception of the treatment; one was well as long as she took small doses of the drug, but the symptoms gradually returned when the drug was stopped. The remaining patient was in no way improved although she was no worse as a result of the treatment. The treatment consisted of the internal administration of corpus luteum extract in doses of two grains three times daily for periods varying from one to six months, the average being three months. This was supplemented by appropriate local treatment such as the judicious use of hot douching and local applications of a solution of magnesium sulphate in glycerine.

Two cases were treated in which the natural menopause was approaching. In one the chief symptom was pruritus of the vulva and relief was obtained after the administration of six grains of corpus luteum daily for two months; the other case presented vasomotor symptoms which disappeared after the administration of corpus luteum in a daily dose of fifteen grains for one month, at the end of which time the menses returned and lasted six days—this being the first menstruation that the patient had had in four months.

In one case of surgical menopause with marked symptoms, there was no improvement as the result of treatment; it might be stated, however, that this patient had been operated upon eighteen months before the authors saw her.

The last subdivision consists of two cases of functional insufficiency of the ovary, only one of which was traced. In this case, the patient had an infantile uterus and complained of bilateral ovarian pain at the time of the menses, associated with a very scanty flow. Her symptoms were relieved by taking six grains of corpus luteum daily for two months.

Thyroid extract is probably the most abused of the organic extracts. The author believes that the action of

thyroid is synergistic with that of the ovary and it is indicated in cases where either the thyroid or ovarian secretion is below normal. In cases of ovarian hyposecretion, the first choice is always corpus luteum, but many times the cost of this drug is prohibitive and in such cases thyroid extract has been substituted with the hope that a good effect would be produced. The results, however, have been only moderately encouraging. It was given in three cases of pelvic inflammatory disease. One was markedly improved, another was moderately improved, while the third showed no improvement. In two cases of natural menopause, there was seen a great improvement in one and no improvement in the other; a case of surgical menopause was slightly improved while taking the drug but the symptoms returned after the cessation of its administration. In two cases diagnosed as ovarian hyposecretion without demonstrable cause, associated with amenorrhea, the results were brilliant. One of these cases, a girl of eighteen years, who had never menstruated, who was physically and mentally a child of twelve years, showed improvement from the very beginning. She became mentally active, began menstruating, and showed enlargement of the breasts, growth of pubic hair, and other secondary sexual characteristics. Here also, as in corpus luteum therapy, the authors use small doses of thyroid extract, never over six grains daily and often only one and a half grains a day. The average duration of these treatments has been about two months.

The authors believe that the secretion from the pituitary body is antagonistic to that of the ovary in so far as its effect upon the uterus is concerned and the chief indication for the use of pituitary substance has been in the treatment of uterine bleeding of uncertain etiology. They have had six cases in which they have tried the drug, but unfortunately have been able to trace only four of them. Two of the patients were suffering from menarchial hemorrhages (profuse menorrhagia and metrorrhagia occurring at puberty) and were both promptly cured by the administration of small doses of pituitary substance, one receiving one-half grain three times daily, and the other one grain three times daily. Another case of closely allied origin was that of a young woman twenty years old, who was having profuse menorrhagia, severe enough to confine her to bed for two days at each period and the menses were recurring every two weeks. She was showing signs of weakness as the result of the loss of blood. The history and pelvic examination threw no light on the subject. A diagnosis of ovarian menorrhagia was made and she was given one grain of pituitary substance three times daily. Her last report was that she had not

menstruated for three weeks and her general condition was markedly improved.

In conclusion, the authors emphasize the importance of individualization in the study and treatment of these cases. —E. N.

(THYROID) Treatment of Dysthyroidism by Roentgen Rays. Palmer (M. B.) N. Y. State J. Med. 1917, xvii, 425.

Provided the case be given the proper treatment nearly every case of dysthyroidism should show improvement and others should be symptom free.

Cases which are to be operated upon should have at least one treatment four weeks previous to operation and unless imperative, the second treatment should be given in cases showing a high pulse rate.

The avoidance of surgery is essential in a large proportion of cases showing toxic symptoms.

Large goitres giving no symptoms of dysthyroidism should best be removed by the surgeon, rather than be given Roentgen treatments. M. B. G.

(ENDOCRINE GLANDS) The Pathogenesis of Some Non-Psychogenetic Types of Functional Nervous Disorder. Williams, T. A., Alienist and Neurologist, 1916, xxxvii, No. 4.

Of the illustrative cases two are of endocrine interest.

The first had been diagnosed and treated for two years for neurasthenia. The chief symptoms were drugged sensation, inertia, congested head, neuralgia, sensitiveness to coffee and digitalis, gastric contraction, impotence, pilocarpine vagotropism, positive Abderhalden reaction to pituitary, marked enlargement of the sella turcica, and the sphenoidal sinus. The diagnosis was dyspituitarism. Therapy by didymin was unsuccessful; other extracts gave further discomfort.

Case II. Paresthenia and ocular asthenia, with neuralgia pseudo-paralysis, history of migraine and ereutophobia, tremor, great fatigueability, hyperhydrosis, slight dermatographia, mild tachycardia, enothalmos, marked increase of weight, slight leucocytosis, tenderness of subcutaneous fat.

Diagnosis, pluriglandular dystrophy.

Therapeutics, mixed hormones of adrenal, pituitary, thyroid, and ovary; great improvement, but a relapse in three months aggravated by pituitary; but great improvement under adrenal since publication of the cases. (Author's abstract.)

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